CORNELL UNIVERSITY.

Department of Chemistry.

On the Constitution of Galleïn and Coeruleïn.

A DISSERTATION

Submitted to the University Faculty for the Degree of Doctor of Philosophy.

BY

CHARLES EDWARD BREWER.

1900.

EASTON, PA.:
THE CHEMICAL PUBLISHING COMPANY.
1900.

CORNELL UNIVERSITY.

Department of Chemistry.

On the Constitution of Galleïn and Coeruleïn.

A DISSERTATION

Submitted to the University Faculty for the Degree of Doctor of Philosophy.

BY

CHARLES EDWARD BREWER.

1900.

EASTON, PA.:
THE CHEMICAL PUBLISHING COMPANY.
1900.

ACKNOWLEDGMENT.

This work was undertaken at the suggestion of Dr. W. R. Orndorff and prosecuted with his constant coöperation. I desire to express my grateful appreciation not only of his unfailing and sympathetic interest in the work, but also of his many kindnesses shown me personally.

I acknowledge gladly my indebtedness to Dr. A. C. Gill, of Cornell University, for accurate description and measurement of crystals. My thanks are tendered also Professors Caldwell and Dennis for their uniform kindness to me.

May, 1900.

HISTORICAL.

I. GALLEÏN.

It was in 1871 that Adolph von Baeyer[1] discovered galleïn. He made it by heating together phthalic anhydride and pyrogallol. The product was purified by dissolving in alcohol and precipitating with water. He described it as a solid, red by reflected light, blue by transmitted light. Later[2] he described it as a brown-red powder, or small metallic-green crystals. He found it to be soluble in alcohol with dark-red color, in potassium hydroxide with splendid blue color, which, however, it loses on continued exposure to air. In ammonium hydroxide it dissolves with purple color.

He regarded the compound as derived from pyrogallol by loss of water according to the reaction:

$$\underset{\text{Pyrogallol.}}{3C_6H_6O_3} = \underset{\text{Galleïn.}}{C_{18}H_{14}O_7} + 2H_2O.$$

The results of his analysis of the new compound agreed with the above formula.

Later[3] he tried the action of phthalic anhydride upon other hydroxyl derivatives of benzene, among them phenol and resorcin. He found that these reacted in a manner similar to that of pyrogallol, phenol giving phenolphthaleïn and resorcin giving fluoresceïn. From the analysis of phenolphthaleïn he was led to consider it as made up of one residue of phthalic anhydride and two residues of phenol, and represented the reaction thus:

$$\underset{\substack{\text{Phthalic}\\\text{anhydride.}}}{C_8H_4O_3} + \underset{\text{Phenol.}}{2C_6H_6O} = \underset{\text{Phenolphthaleïn.}}{C_{20}H_{14}O_4} + H_2O.$$

Fluoresceïn, from its similarity to phenolphthaleïn and also from the results of analysis, he regarded as derived from 1 molecule of phthalic anhydride and 2 of resorcin, thus:

[1] Ber. d. chem. Ges., 4, 457.
[2] *Ibid.*, 4, 555.
[3] *Ibid.*, 4, 658.

$$C_8H_4O_3 + 2C_6H_6O_2 = C_{20}H_{12}O_5 + 2H_2O.$$

Phthalic anhydride. Resorcin. Fluoresceïn.

A study of these reactions led him to change his views of the reaction by which galleïn was made.[1] He regarded it as made according to the following equation :

$$C_8H_4O_3 + 2C_6H_6O_3 = C_{20}H_{12}O_7 + 2H_2O.$$

Phthalic anhydride. Pyrogallol. Galleïn.

Thus it would be the phthaleïn of pyrogallol.

By reduction in alkaline solutions by zinc dust, Baeyer discovered that phthaleïns lose color and are converted into closely related compounds which he called phthalins.

The structure of galleïn is so closely related to that of the phthaleïns in general that a summary of work done in establishing the structure of the latter is necessary for an intelligent study of the structure of the former.

Fluoresceïn was the first of the phthaleïns to be investigated and have assigned to it a constitutional formula. The work was done by Baeyer and his assistants.[2] Fluoresceïn was made by heating together resorcin and phthalic anhydride. The purified product proved to be a yellow crystalline powder which dissolved in alkalies with a beautiful green fluorescence. Results of the analysis of the compound pointed to formula $C_{20}H_{14}O_6$ as representing its composition.

On the other hand, E. Fischer[3] prepared *pure* fluoresceïn by first making its acetate, purifying it by recrystallization, and then saponifying it with alcoholic caustic potash. Fluoresceïn thus prepared was analyzed and the results pointed to $C_{20}H_{12}O_5$ as its formula.

Baeyer's next object was to determine the number of hydroxyl groups contained in fluoresceïn. This he did by making its acetyl and benzoyl derivatives in the usual way. He found that in each case two acid residues were introduced —that the compounds formed were the diacetate and the di-

[1] Ber. d. chem. Ges., 4, 663.

[2] Ann. Chem. (Liebig), 183, 2ff.

[3] Ber. d. chem. Ges., 7, 1211.

benzoate of fluoresceïn. Further, he made what he termed the monoethyl and the diethyl ethers of fluoresceïn, and the dichloride. The fact that in all but one of the derivatives thus far mentioned two substituting atoms or groups replaced hydroxyls or the hydrogen atoms of these hydroxyl groups, pointed to the presence of two hydroxyl groups in fluoresceïn.

Quite a series of substitution-products in which two or more hydrogen atoms were replaced, gave information of other characteristics of fluoresceïn. Thus, dinitro and tetranitro fluoresceïn; mono-, di-, and tetrabrom fluoresceïn (eosin); salts of eosin; erythrin (ethyl ester of eosin); diethyl ether of eosin—all followed in rapid succession.

By fusing fluoresceïn with potassium hydroxide Baeyer found that decomposition follows in two stages. First, he obtained what he called monoresorcin phthaleïn, to which he gave the formula:

$$C_6H_4\left<\begin{array}{l} COC_6H_3\left<\begin{array}{l}OH\\ OH.\end{array}\right. \\ COOH\end{array}\right.$$

When heated further this compound yielded, besides resorcin, benzoic acid and carbon dioxide. The last two compounds came from the phthalic acid residue.

As the result of his investigation, he concluded that without doubt fluoresceïn was a diketone and should be given the formula:

$$C_6H_4\left<\begin{array}{l} COC_6H_3\left<\begin{array}{l}OH\\ \end{array}\right. \\ \qquad\qquad\quad >O \\ COC_6H_3\left<\begin{array}{l} \\ OH\end{array}\right.\end{array}\right. .$$

The formation of the anhydride between the hydroxyl groups in the resorcin residues was, he said, in harmony with an observation made by him in the preparation of phenolphthaleïn. Two compounds were in reality formed in the synthesis of phenolphthaleïn—one a phthaleïn proper, the other a phthaleïn anhydride. The relation of the two is expressed in the formulas:

$$C_6H_4\left<\begin{array}{l} COC_6H_4OH \\ COC_6H_4OH \end{array}\right. \quad \text{and} \quad C_6H_4\left<\begin{array}{l} COC_6H_4 \\ COC_6H_4 \end{array}\right> O.$$

Phenolphthaleïn. Phenolphthaleïn anhydride.

Fuoresceïn would, therefore, be a dihydroxyl derivative of the above anhydride form,

E. Fischer[1] made the phthaleïn of orcin,

$$C_6H_3\left<\begin{array}{l} CH_3\ (1) \\ OH\ \ (3) \\ OH\ \ (5) \end{array}\right. ,$$

and found it to resemble fluoresceïn very closely. He made a series of derivatives similar to those made from fluoresceïn by Baeyer. As a result of his study of this new phthaleïn he gave it a formula in harmony with that of Baeyer for fluoresceïn, as follows :

$$\begin{array}{lll} & & \diagup CH_3 \\ & COC_6H_2 & —OH \\ C_6H_4\left<\vphantom{\begin{array}{l}a\\a\end{array}}\right. & & \rangle O \\ & COC_6H_2 & —OH \\ & & \diagdown CH_3 \end{array} .$$

Baeyer's view of the structure of fluoresceïn, (and of the phthaleïns in general), was modified in some essential points as a result of his further study of phenolphthaleïn.[2] A difficulty arose in explaining by the accepted diketone formula the action of melted alkalies on phenolphthaleïn. Such action resulted in the formation of dioxybenzophenone,

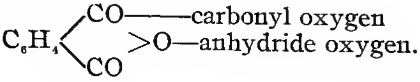
$$CO\left<\begin{array}{l} C_6H_4OH \\ C_6H_4OH \end{array}\right. ,$$

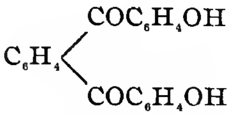
and benzoic acid. According to the diketone formula, this would require a shifting of one of the C_6H_4OH groups. It occurred to him that this decomposition could easily be explained by assuming that it is one of the carbonyl oxygen atoms and

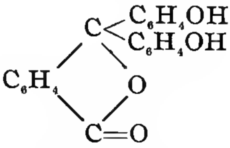
[1] Ann. Chem (Liebig), 183, 63.

[2] *Ibid.*, 202, 36.

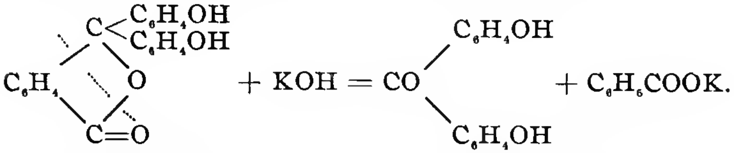
not the anhydride oxygen of the phthalic anhydride that is replaced by two phenol residues. The difference is seen in the following structural formulas:



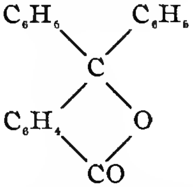

Diketone formula.


New formula.

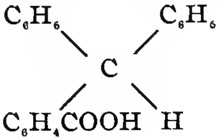
The explanation of the formation of dioxybenzophenone is very difficult by the diketone formula, while it is quite simple by the new one, as will appear from the following scheme:


Phenolphthaleïn. Dioxybenzophenone.

Baeyer found further evidence for the new formula in the synthesis of phenolphthaleïn by a method which can leave no doubt as to its structure and genetic relations. He treated benzene with phthalic anhydride in presence of aluminium chloride and obtained diphenylphthalid:

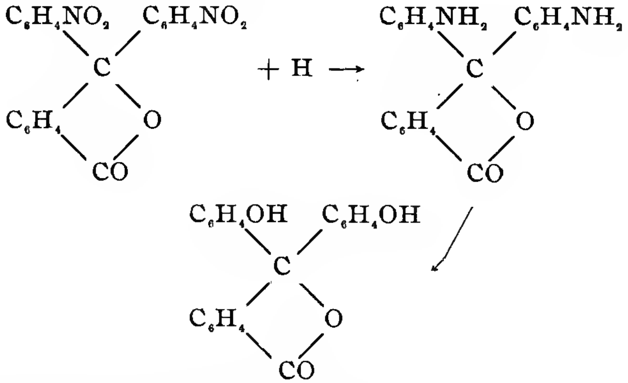


This, on reduction with zinc dust, gave triphenylmethane carbonic acid:

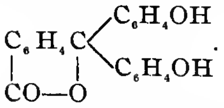


This, when heated with a base, lost carbon dioxide and yielded triphenyl methane.

Having thus established the relation of diphenylphthalid to triphenyl methane, his next task was to show the relation of phenolphthaleïn to diphenylphthalid. Diphenylphthalid treated with nitric acid gave a dinitro derivative which, by reduction, yielded a diamido derivative. Diamidodiphenylphthalid, by the action of nitrous acid and water, was converted into dioxydiphenylphthalid. These changes are shown in the following formulas :



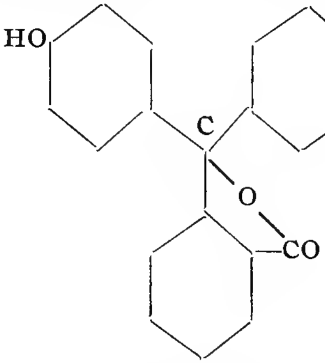
This dioxydiphenylphthalid proved to be identical in every respect with phenolphthaleïn, made by heating together phthalic anhydride and phenol in presence of zinc chloride. This he showed not only by comparison of the phthaleïn from the two sources but also by comparison of a number of derivatives of each. Thus its connection with triphenyl methane was clearly established and its structure shown to be



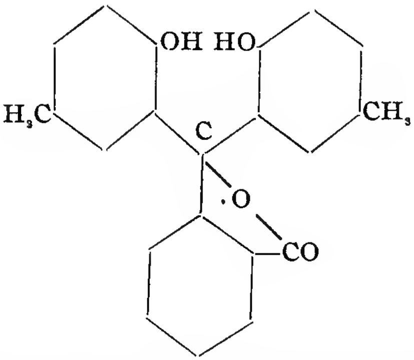
Dioxydiphenylphthalid, or phenolphthaleïn.

Having shown the relation of phenolphthaleïn to triphenylmethane, efforts were made to establish the relation of its hydroxyl groups to the methane carbon atom. As a working

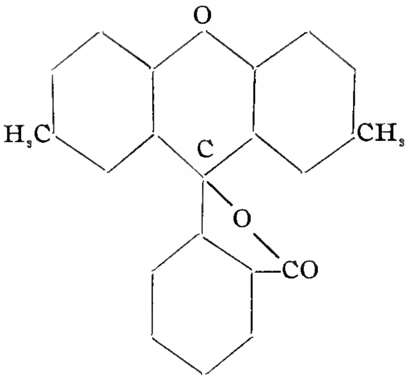
hypothesis Baeyer suggested that the hydroxyl groups were *para* to the methane carbon atom. He was led to this conclusion from the observation that phenols, with the para position already occupied, yielded not true phthaleïns but their anhydrides. In such cases the hydroxyls are ortho to the methane carbon atom and being at the same time in greater proximity to each other, lose a molecule of water and form an anhydride. In other words, the para relation between the hydroxyl groups and the methane carbon atom is the one preferred, thus:



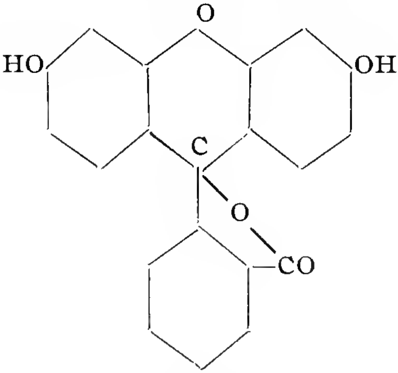
If, however, the para position in the phenol is already occupied, as for instance in *p*-cresol, then the ortho position is preferred, thus:



But this loses a molecule of water and becomes the anhydride :



In view of this work in establishing the constitution of phenolphthaleïn, Baeyer[1] was led to abandon the diketone formula for fluoresceïn also and to assign to it a constitution analogous to that of phenolphthaleïn, and hence it is to be regarded as a dioxy-derivative of phenolphthaleïn anhydride :



Such was the state of our knowledge of the phthaleïns when, in 1881, Karl Buchka[2] began his investigation of galleïn. He first made the compound according to Baeyer's directions and found its properties to be those given by him. He went further and made several derivatives, among them were the tetracetate, the tetrabenzoate, dibromgalleïn, and the dibrom-

[1] Ann. Chem. (Liebig), 212, 351.
[2] *Ibid.*, 209, 251.

galleïn tetracetate. He made the acetate by mixing galleïn and fused sodium acetate in equal proportions, with three to four times as much acetic anhydride and boiling for three or four hours. On cooling, the mass solidified, was washed well with water, and recrystallized from benzene. It proved to be colorless, soluble in alcohol, glacial acetic acid, and acetone ; insoluble in ether. It was also easily saponified by alkalies, even in the cold, and had a melting-point of 247°–248° C.

He reduced galleïn in alkaline solution by means of zinc dust, and found that by observing certain precautions he succeeded in making a compound intermediate between Baeyer's galleïn and gallin. He dissolved galleïn in a solution of potassium hydroxide and decolorized with zinc dust, *in the cold*, acidified with sulphuric acid, extracted with ether, and after evaporating off the ether had left a slightly red oil which soon solidified. A remarkable property of this compound he found to be that it is converted by heating with acetic anhydride alone into an acetate that is identical with the galleïn tetracetate made by treatment of galleïn with sodium acetate and acetic anhydride. He called this intermediate reduction-product hydrogalleïn.

In order to make gallin he dissolved galleïn in ammonium hydroxide, heated to boiling, and added zinc dust by degrees until reduction had reached the proper point, acidified with sulphuric acid, filtered, cooled in absence of air, and extracted with ether. After evaporation of ether an oil was left which soon became solid. It differed from hydrogalleïn in that it condensed with concentrated sulphuric acid in the cold to a phthalidin, had acid properties, and when acetylized yielded a product which melted at 220° C.

By long-continued reduction in either acid or alkaline solution he obtained from galleïn a still lower reduction-product, which he called gallol. This formed a pentacetate when treated with acetic anhydride.

Buchka denied the correctness of Baeyer's formala ($C_{20}H_{12}O_7$) by reason especially of the reduction-products which he obtained. The compound which he obtained by reduction with potassium hydroxide and zinc dust in the cold did not act at all

like a phthalin would be expected to act—it had no acid properties and was not condensed to a phthalidin by sulphuric acid. In view of the existence of this intermediate reduction-product of galleïn, which he named hydrogalleïn, he was led to the conclusion that, in the process of making, galleïn suffers slight oxidation, resulting in loss of two hydrogen atoms and the formation of a quinone. He gave, therefore, to galleïn the formula:

$$\begin{array}{l} C_6H_4C\left\langle\begin{array}{l} C_6H_2OH \\ \qquad >O_2 \\ C_6H_2OH \end{array}\right\rangle O. \\ \ | \qquad\ \ | \\ CO{-}O \end{array}$$

A precedent for this he found in the formation of cedriret,

$$\begin{array}{l} C_6H_2(OCH_3)_2O \\ \ | \qquad\qquad\qquad\ | \\ C_6H_2(OCH_3)_2O \end{array},$$

from pyrogallol dimethyl ether by oxidation.

To hydrogalleïn he assigned the formula:

$$\begin{array}{l} C_6H_4C\left\langle\begin{array}{l} C_6H_2(OH)_2 \\ \\ C_6H_2(OH)_2 \end{array}\right\rangle O, \\ \ | \qquad\ \ | \\ CO{-}O \end{array}$$

as it is formed from galleïn by the assumption of hydrogen; and to gallin the formula:

$$\begin{array}{l} C_6H_4CH\left\langle\begin{array}{l} C_6H_2(OH)_2 \\ \\ C_6H_2(OH)_2 \end{array}\right\rangle O. \\ \ | \\ COOH \end{array}$$

And gallol was represented thus:

$$\begin{array}{l} C_6H_4CH\left\langle\begin{array}{l} C_6H_2(OH)_2 \\ \\ C_6H_2(OH)_2 \end{array}\right\rangle O. \\ \ | \\ CH_2OH \end{array}$$

The fact that galleïn forms a *tetra*acetate and a *tetra*benzoate, he says, might be used as an argument against the formula as given by him, since one would expect a compound with such a formula to yield a *di*acetate and a *di*benzoate. Analyses of the

compounds, however, leave no doubt that four acetyl, or benzoyl, groups have been introduced. The properties of these derivatives, also, preclude the possibility of their containing a quinone group. He adds,[1] "Man muss daher, *wenn man an der Annahme einer Chinonbildung im Galleïn festhalten will*, eine Sprengung dieser Bindung bei der Aetherbildung voraussetzen." Such a reaction, he continues, is not without precedent. Sarauw[2] has made hydroquinone diacetate from quinone by action of acetic anhydride and sodium acetate upon it. Graebe[3] has also made the diacetate of tetrachlorhydroquinone by the action of acetyl chloride upon chloranil.

In 1892 Herzig[4] repeated a part of Buchka's work and obtained results which do not entirely agree with Buchka's statements. He was led to this investigation by a study of certain other compounds of the phthaleïn series. Graebe and Caro[5] had found that rosolic acid heated in a sealed tube with acetic anhydride forms an acetate, not of rosolic acid, but of its leuco derivative. This suggested the idea to Herzig that the action of acetic anhydride upon the phthaleïns is not one of simple acetylization but of reduction as well. This idea was supported by the fact that the melting-points of the acetates of the phthaleïns and their corresponding phthalins are very close together. The question which presented itself was, do the phthaleïns and the corresponding phthalins give the same product when acetylized? To answer it he prepared carefully some fluoresceïn acetate and also some fluorescin acetate, and subjected them not only to the melting-point test but to chemical tests as well. He found that while these two acetates have almost exactly the same melting-point (fluoresceïn acetate 200°–201° C., fluorescin acetate 200°–202° C.), they react very differently towards a dilute solution of alkali. Fluoresceïn acetate dissolves very slowly—only as it is saponified—and after several hours unchanged fluoresceïn acetate may be filtered out. Fluorescin acetate, on the other hand, dis-

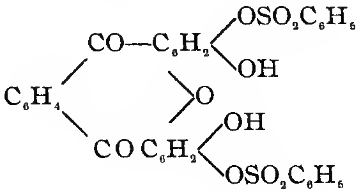
1 Ann. Chem. (Liebig), 209, 255.
2 Ber. d. chem. Ges., 12, 680.
3 Ann. Chem. (Liebig), 146, 13.
4 Monatsh. Chem., 13, 425.
5 Ann. Chem. (Liebig), 179, 198.

solves in dilute alkalies at once, and, if acidified, unchanged fluorescin acetate will be precipitated. They are clearly different substances. Inasmuch as Buchka had not subjected his hydrogalleïn acetate to such a test as this but had relied upon a melting-point test to prove its identity with galleïn acetate, it occurred to Herzig to prepare galleïn and hydrogalleïn acetates in order to determine whether they agreed in chemical conduct as they did in melting-point according to Buchka.

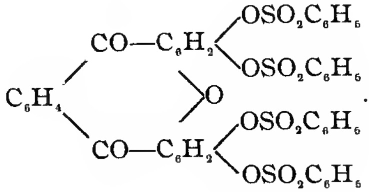
As a result of this work he found, in the first place, that galleïn acetate melted at 237°–238° C., instead of at 247°–248° C., as given by Buchka. In the next place, Herzig's efforts to make hydrogalleïn and its acetate did not succeed. He purified his galleïn carefully by converting it first into the acetate, recrystallizing this, and saponifying with potassium hydroxide. This purified product he dissolved in potassium hydroxide solution and reduced in the cold by means of zinc dust. The reduced product thus made he acetylized with acetic anhydride and obtained a product that melted at 211°–213° C. and dissolved in potassium hydroxide solution without saponification. It could not, therefore, have been identical with galleïn acetate. Herzig assumed that it was the same compound as Buchka's gallin tetracetate, which, according to Buchka, melts at 220°, though he did not make the latter compound in order to compare the two side by side, nor did he give any analyses. He concludes the account of his investigation by saying : "Buchka scheint nach seiner Beschreibung eine grössere Menge des Hydrogalleïns in der Hand gehabt zu haben, und es können daher meine beiden negativen Befunde vorläufig die Existenz desselben nicht in Frage stellen. Allerdings glaube ich, dass die Darstellung des Hydrogalleïns nicht so einfach ist, wie sie Buchka beschreibt und dass noch andere Vorsichtsmassregeln nothwendig sind, die der genannte Autor entweder nur unbewusst eingehalten oder in seiner Arbeit zu erwähnen vergessen hat. Ebenso halte ich es vorläufig nicht für ausgeschlossen, dass die Identität der Acetylproducte des Galleïns und Hydrogalleïns nur auf Grund der Schmelzpunkte ausgesprochen wurde, während sie sich in Bezug auf die Löslichkeit in Alka-

lien von einander so unterscheiden können, wie Acetylfluoresceïn von Acetylfluorescin."

Galleïn diphenylsulphonate and tetraphenylsulphonate have also been made by M. Georgescu.[1] The galleïn diphenylsulphonate was made by treating an alkaline solution of galleïn with benzene sulphonchloride until the color of the solution becomes greenish-yellow. In solution the compound is dichroic, green by reflected light, reddish-yellow by transmitted light. He assigned to it the formula :

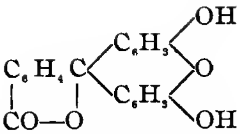


Gallein tetraphenylsulphonate was made by the same investigator by treating an alkaline solution of galleïn with benzene sulphonchloride in excess. A brown precipitate, insoluble in alkalies, was thrown down, which, when purified, was nearly colorless and melted at 187°–188° C. To this he gave the formula :

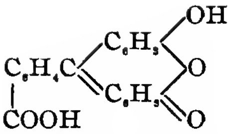


The period between 1891 and 1897 was one of great activity in researches upon the constitution of the phthaleïns. This was stimulated by a suggestion as to the structure of fluoresceïn on the part of Bernthsen, who first gave the quinoid structure to this compound instead of the lactoid structure proposed by Baeyer. The relation of the two may be seen in the following formulas for fluoresceïn :

[1] Buletinul Societătii De Sciinte Fizice, 1, 215 (1892).



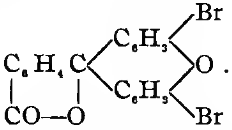
Lactoid structure.



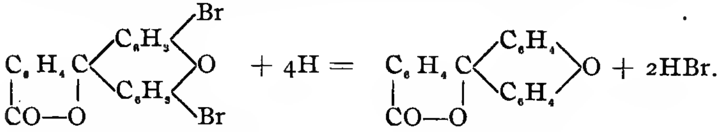
Quinoid structure.

Bernthsen[1] suggested that in free condition as well as in such derivatives as have no color the structure is to be represented by the lactoid formula, while in such derivatives as possess color the structure is best represented by the quinoid arrangement. The discussion for the next few years centered largely around this question—the lactoid *versus* the quinoid arrangement—and one other, the relation of the hydroxyl groups to the methane carbon atom.

Richard Meyer[2] showed the connection between fluoresceïn and fluoran (phenolphthaleïn anhydride)—that fluoresceïn is in reality dioxyfluoran. This he did in two ways. First, by treating fluoresceïn with phosphorus pentabromide he obtained fluoresceïn dibromide :

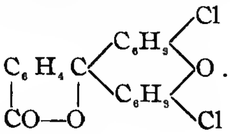


This he reduced by nascent hydrogen and obtained fluoran :



Fluoresceïn dibromide. Fluoran.

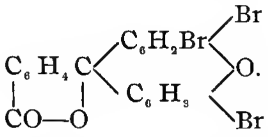
Second, by action of phosphorus pentachloride on fluoresceïn he made fluoresceïn dichloride :



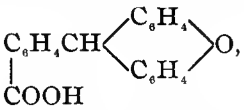
[1] Chem. Ztg., 16, 1956.

[2] Ber. d. chem. Ges., 25, 1385.

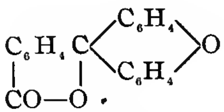
This, in turn, when treated with phosphorus tribromide gave him monobromfluoresceïn dibromide :



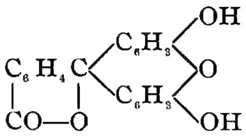
When this is treated with alcoholic caustic soda and zinc dust it is reduced to an acid to which he assigns the formula :



and names hydrofluoranic acid. The same acid is formed when fluoran is heated with alcoholic caustic soda and zinc dust There could be no doubt, therefore, that the relation of fluoresceïn to fluoran was expressed in the formulas :

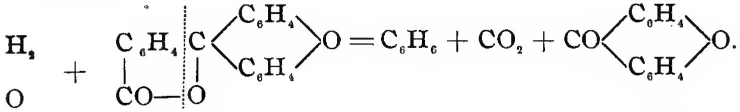


Fluoran.



Fluoresceïn.

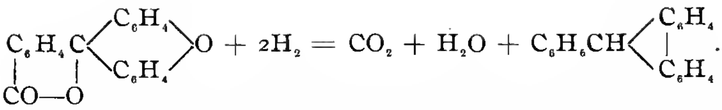
Meyer next applied himself to the task of establishing the structure of fluoran.[1] He found that fluoran, when heated with lime, decomposes into benzene, carbon dioxide, and xanthone :



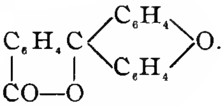
Fluoran. Xanthone.

Again, he distilled fluoran with soda-lime and zinc dust[2] and found the products to be water, carbon dioxide, and diphenylene phenylmethane.

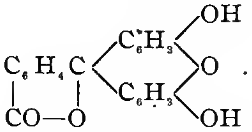
[1] Ber. d. chem. Ges., 25, 2118.
[2] *Ibid.*, 25, 3586.



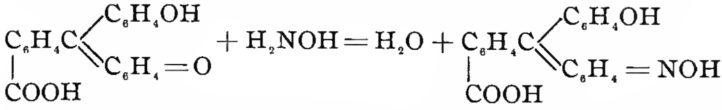
The reactions of fluoran with lime and with soda-lime and zinc dust can most readily be explained on the assumption that it has the structure :



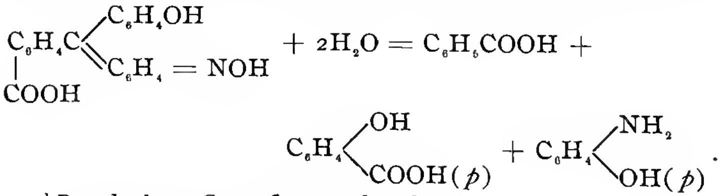
Fluoresceïn, as a dioxy-derivative, would be :



Friedländer[1] contributed some observations which seemed to confirm the views of Baeyer as to the relation of the hydroxyl groups of phenolphthaleïn to its methane carbon atom. This he did in the preparation of the so-called phenolphthaleïn oxime and a study of its decomposition-products. Phenolphthaleïn in alkaline solution reacts with hydroxylamine as a quinone or a ketone would act, forming an oxime according to the reaction :



This oxime is a light-yellow product, dissolves in alkalies with yellow color, reprecipitated by acids. Its decomposition-products were especially interesting. Fused with caustic soda, it yielded benzoic acid, *p*-oxybenzoic acid, and *p*-amidophenol :



[1] Ber. d. chem. Ges., **26**, 172 and 2258.

The oxime, when boiled with dilute sulphuric acid, forms *p*-oxy-*o*-benzoylbenzoic acid and *p*-amidophenol :

$$\begin{array}{l} C_6H_4C\left\langle\begin{array}{l} C_6H_4OH \\ C_6H_4 = NOH \end{array}\right. \\ | \\ COOH \end{array} + H_2O =$$

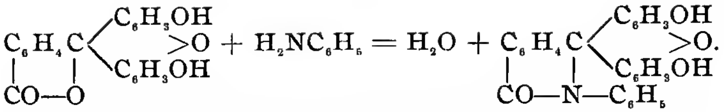
$$C_6H_4\left\langle\begin{array}{l} COOH\,(o) \\ COC_6H_4(OH)\,(p) \end{array}\right. + C_6H_4\left\langle\begin{array}{l} NH_2 \\ OH\,(p) \end{array}\right. .$$

From these results it would seem that the hydroxyl groups are *para* to the methane carbon atom, as first suggested by Baeyer.

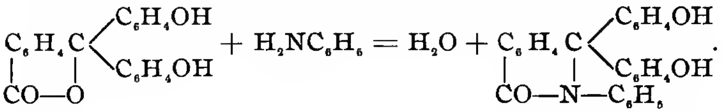
Friedländer, in testing the oxime reaction with other phthaleïns, found that it took place most readily in those cases in which the quinoid structure was made known by color. This applied to derivatives as well as to the phthaleïns themselves. For example, the dark-blue or violet alkaline solution of tetrabromphthaleïn reacted easily with hydroxylamine, but not so the light-yellow solution of the di- or tetranitrophenolphthalein. It was of special interest to observe that the solution of fluoresceïn in dilute alkalies—which is reddish-yellow—did not react with hydroxylamine, while the deep-violet solution of fluoresceïn in hot concentrated alkalies combines with that reagent easily. These facts, he claimed, supported the *lactoid* formula for free fluoresceïn and its stable salts, at the same time pointing to the *quinoid* structure for such derivatives as possess marked color.

O. Fischer and Hepp[1] made fluoresceïn anilide by boiling together fluoresceïn, aniline, and aniline hydrochloride. The excess of aniline was removed by adding excess of alkali and distilling with steam. The residue was crystallized from alcohol. The crystals were colorless, dissolving without color in alcohol and glacial acetic acid, in alkalies with green fluorescence. On account of its lack of color they concluded that it could not have the quinoid structure and wrote the equation expressing its formation as follows :

[1] Ber. d. chem. Ges., 26, 2236.

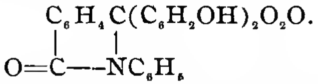


By a reaction similar to that used in the preparation of fluoresceïn anilide, Albert[1] made phenolphthaleïn anilide :



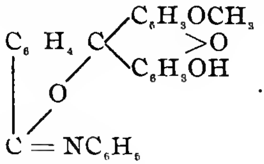
This anilide is also colorless and agrees in its properties generally with the anilide of fluoresceïn.

Again, by the same reaction, Albert[2] made galleïn anilide and represented the structure in this way :



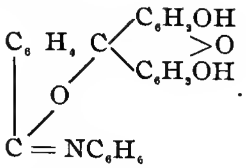
He found it to be colorless, soluble in alkalies without color, and with methyl iodide in a sealed tube at 100°, formed a dimethyl derivative.

A year later O. Fischer and Hepp[3] made the anilide of fluoresceïn monomethyl ether. In their study of this compound they were led to modify their view of the structure of phthaleïn anilides. Up to this time these had been represented as phthaleïns in which the *anhydride* oxygen of the phthalic acid residue was replaced by an aniline residue. The authors now represented them as phthaleïns in which the *carbonyl* oxygen is replaced by the aniline residue. Thus, for the anilide of fluoresceïn monomethyl ether they gave the formula :

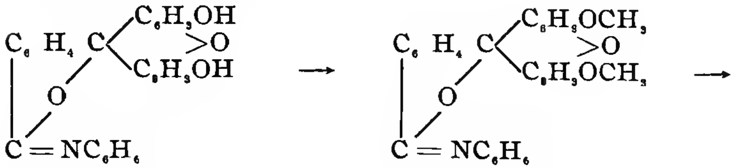


[1] Ber. d. chem. Ges., 26, 3077.
[2] *Ibid.*, 27, 2793.
[3] *Ibid.*, 28, 398.

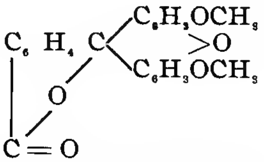
And for fluoresceïn anilide :



They assign no reason for either formula. That the anilides above referred to have not the quinoid structure was shown by converting them into methyl ethers, splitting off the aniline residue, which resulted in the formation of a *colorless* ether, as shown by the following formulas :



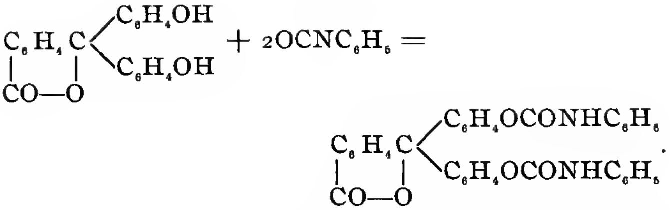
Fluoresceïn anilide. Dimethylfluoresceïn anilide.



Dimethyl ether of fluoresceïn.
(Colorless.)

Haller and Guyot[1] submitted evidence for the *lactoid* structure of both phenolphthaleïn and fluoresceïn in the free state by making diphenyl carbamate derivatives of each. This was done by simply heating the phthaleïn with phenyl isocyanate to 130°, and recrystallizing the product from benzene. There resulted a colorless compound, stable with boiling water, but easily decomposed by alkalies, regenerating the corresponding phthaleïn. They represented the reaction for phenolphthaleïn thus :

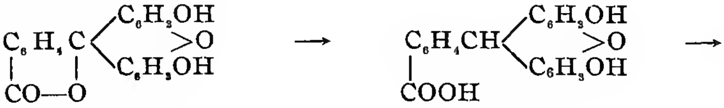
[1] Compt. rend., 116, 479.



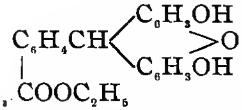
Phenolphthaleïn bis-phenylcarbamate.

Fluoresceïn reacted similarly, yielding fluoresceïn bis-phenyl carbamate. Now, since phenyl isocyanate reacts with hydroxyl groups but not with carbonyl groups, and since two phenyl isocyanate residues are introduced into the molecule, it is shown that in *free* phenolphthaleïn, as well as in *free* fluoresceïn, there are *two* hydroxyl groups.

A valuable contribution to the question of the structure of the phthaleïns was made by Nietzki and Schröter[1] in their work on the ethyl ethers of fluoresceïn. They succeeded in preparing diethyl ethers of fluoresceïn by reactions that leave no doubt as to their structure. Fluoresceïn was first reduced to fluorescin, and this converted into the ethyl ester in the usual way. The relation of these compounds is shown in the following formulas :

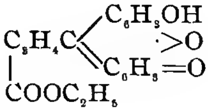


Fluoresceïn. Fluorescin.



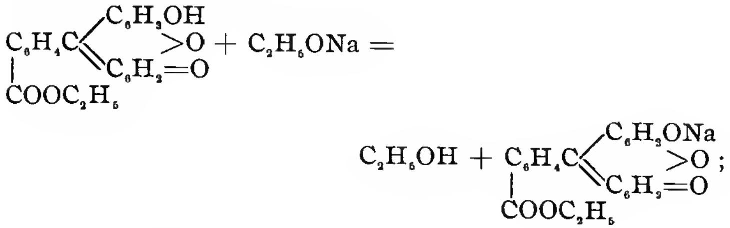
Fluorescin ethyl ester.

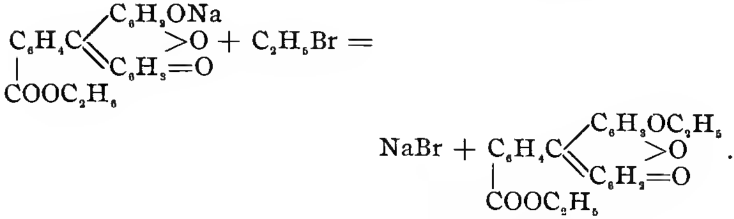
Fluorescin ethyl ester, by oxidation, goes easily into fluoresceïn ethyl ester :



[1] Ber. d. chem. Ges., 28, 44.

This compound has color. When treated with sodium ethylate and ethyl bromide, it undergoes the changes shown in the following equations :

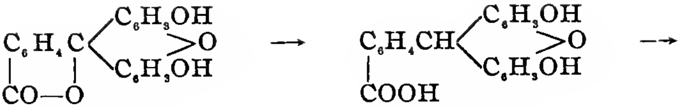




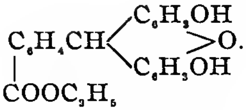
Fluoresceïn diethyl ether.
(Colored.)

That the colored fluoresceïn diethyl ether has the structure assigned to it above—the quinoid structure—is shown not only by the method by which it is prepared, but also by the fact that when carefully saponified it loses the ethyl group combined with the carboxyl group and is converted into a monoethyl ether, which, also, has color.

The same authors (*loc. cit.*) give valuable evidence as to the structure of the *colorless*, or lactoid diethyl ether of fluoresceïn. They reduce fluoresceïn to fluorescin, as in the previous case, esterify, and from the ester, by means of sodium ethylate and ethyl bromide, in the correct proportions, obtain fluorescin triethyl ether, which, on saponification and oxidation, yields *colorless* fluoresceïn diethyl ether. The relations of these products to each other are shown as follows :



Fluoresceïn. Fluorescin.

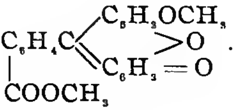


Fluorescin ethyl ester.

Fluorescin triethyl ether. Fluoresceïn diethyl ether. (Colorless.)

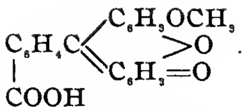
From the methods of preparation, there can be little doubt of the correctness of the above formulas for the two diethyl ethers of fluoresceïn—the colored, or quinoid, and the colorless, or lactoid. It is interesting to note, in this connection, as showing that fluoresceïn reacts as a tautomeric substance, that the same authors[1] succeeded in making both ethers in one operation. The potassium compound of fluoresceïn was heated with ethyl bromide in a closed vessel on the water-bath for several days. The two ethers thus made were separated by fractional crystallization from alcohol, the colored ether being more soluble in that liquid than the colorless ether.

O. Fischer and Hepp[2] made the quinoid (colored) dimethyl ether of fluoresceïn by action of methyl iodide upon an alkaline solution of fluoresceïn in methyl alcohol. It was given the formula:



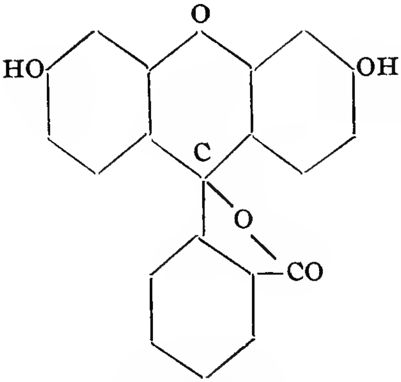
That this is correct was shown by its conduct when treated with an alkali—it saponified and yielded monomethyl fluoresceïn, also colored:

[1] Ber. d. chem. Ges., 28, 49.
[2] *Ibid.*, 28, 396.



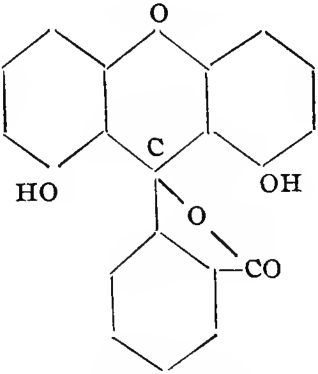
In the year 1895 two investigations were reported which proved the relation of the hydroxyl groups to the methane carbon atom. Graebe had already pointed out that there were only three possible arrangements—remembering that resorcin is a *meta* derivative :

I.



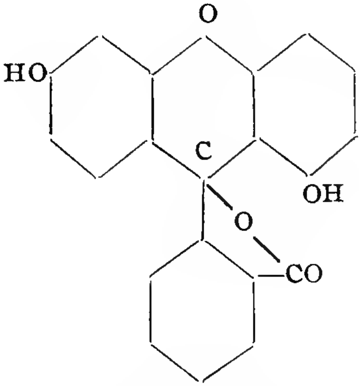
p-p-Symmetrical.

II.



o-o-Symmetrical.

III.

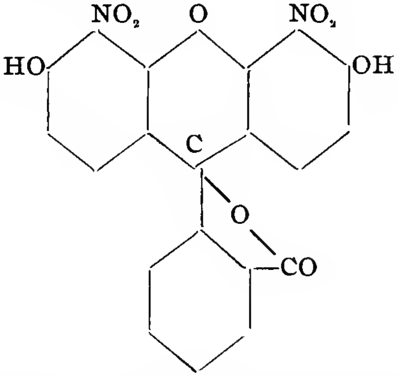


o-p-Unsymmetrical.

Matras[1] made dinitrofluoresceïn, decomposed this with potas-

[1] Chem. Ztg., 19, 408.

sium hydroxide and obtained a volatile nitroresorcin which melted at 85° C. From this it appears that the product was that derivative of resorcin, in which the groups have the relation $OH : NO_2 : OH = 1 : 2 : 3$. The formula for the dinitro-fluoresceïn, then, would be:



Since the nitro group is inserted *between* the hydroxyl groups, formulas II and III are excluded, since in them that position is already occupied. According to this, therefore, the hydroxyl groups are *para* to the methane carbon atom.

To the same conclusion, led an investigation on eosin begun by A. Baeyer[1] and continued by Heller.[2] Baeyer heated eosin with concentrated solution of sodium hydroxide and obtained dibromdioxybenzoyl benzoic acid:

$$\begin{array}{l} C_6H_4C\left\langle\begin{array}{l} C_6HBr_2OH \\ \qquad\qquad >O \\ C_6HBr_2OH \end{array}\right. + H_2O = \\ \,|\qquad\ \ | \\ CO—O \end{array}$$

Eosin.

$$C_6H_2Br_2(OH)_2 + \begin{array}{l} C_6H_4COC_6HBr_2(OH)_2. \\ | \\ COOH \end{array}$$

Dibromresorcin. Dibromdioxybenzoylbenzoic acid.

Heller treated this last compound with warm sulphuric acid

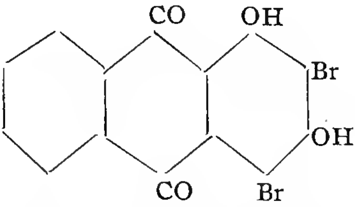
[1] Ann. Chem. (Liebig), 183, 56.

[2] Ber. d. chem. Ges., 28, 312.

and found that it condensed by loss of water to dibromxanthopurpurin, thus :

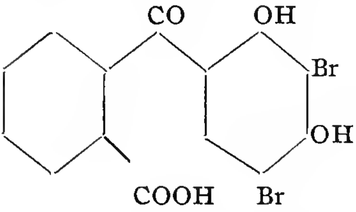
$$\begin{array}{l}\mathrm{C_6H_4COC_6HBr_2(OH)_2-H_2O = C_6H_4}\left\langle\begin{matrix}\mathrm{CO}\\ \mathrm{CO}\end{matrix}\right\rangle\mathrm{C_6Br_2(OH)_2.}\\ \;| \\ \mathrm{COOH}\end{array}$$

Since this is a derivative of xanthopurpurin it must have the structure :

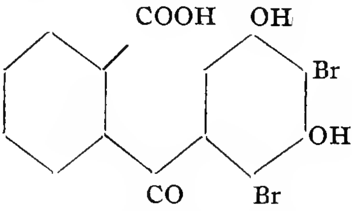


For its hydrated form (see above) there are two alternatives :

I.



II.



But formula II is excluded, since it has been already shown[1] that one of the hydroxyl groups is *ortho* to the phthalic acid residue. It will be seen from formula I that the remaining hydroxyl group is *para* to the phthalic acid residue.

This established the relation of the hydroxyl group to the methane carbon atom *so far as one-half of the molecule* was concerned. It only remained to show that fluoresceïn is symmetrical, that the two resorcin residues sustain the same relation to the molecule. This fact was first established by Baeyer.[2] He found that the dioxybenzoylbenzoic acid, obtained by the decomposition of fluoresceïn, when heated again, loses water with formation of fluoresceïn and phthalic anhydride :

[1] Cf. R. Meyer's work on relation of fluoresceïn to fluoran, p. 18.

[2] Ann. Chem. (Liebig), 183, 25.

$$2C_6H_4\left\langle\begin{array}{l}COC_6H_3(OH)_2\\ COOH\end{array}\right. =$$

Dioxybenzoylbenzoic acid.

$$2H_2O + C_6H_4\left\langle\begin{array}{l}CO\\ CO\end{array}\right\rangle O + \begin{array}{l}C_6H_4C\\ |\qquad |\\ CO{-}O\end{array}\left\langle\begin{array}{l}C_6H_3OH\\ C_6H_3OH\end{array}\right\rangle O.$$

Phthalic anhydride. Fluoresceïn.

Afterwards it was shown[1] that dibromdioxybenzoylbenzoic acid also loses water when heated, forming phthalic anhydride and eosin:

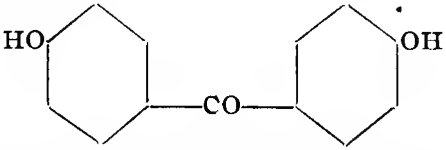
$$2C_6H_4\left\langle\begin{array}{l}COC_6HBr_2(OH)_2\\ COOH\end{array}\right. =$$

$$2H_2O + C_6H_4\left\langle\begin{array}{l}CO\\ CO\end{array}\right\rangle O + \begin{array}{l}C_6H_4C\\ |\qquad |\\ CO{-}O\end{array}\left\langle\begin{array}{l}C_6HBr_2OH\\ C_6HBr_2OH\end{array}\right\rangle O.$$

Eosin.

These syntheses of fluoresceïn and eosin from one product of their decomposition, show clearly that they have a symmetrical structure, and constitute the last link in the chain of evidence for the *para* relation of the two hydroxyl groups to the methane carbon atom.

Baeyer[2] found that when phenolphthaleïn was decomposed by fusing with caustic soda one of the products was dioxybenzophenone. It was afterwards shown that this was *para* dioxybenzophenone:



This proved that in phenolphthaleïn, also, the hydroxyl groups are *para* to the methane carbon atom as in fluoresceïn.

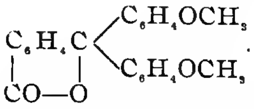
Herzig and H. Meyer[3] advocated the lactoid structure of

[1] Ber. d. chem. Ges., 28, 1576.

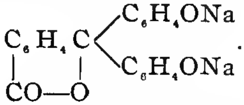
[2] Ann. Chem. (Liebig), 202, 38.

[3] Ber. d. chem. Ges., 28, 3258.

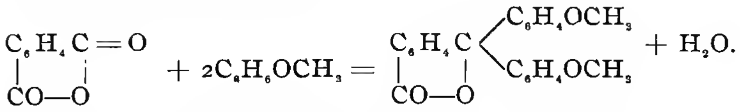
salts of phenolphthaleïn by reason of a colorless dimethyl ether made by them. An alkaline solution of phenolphthaleïn treated with methyl iodide, gave a yield of 85–90 per cent of the colorless, or lactoid, dimethyl ether—a white crystalline substance, insoluble in alkalies. To this they assign the formula:



With this as the structure of the dimethyl ether, the sodium salt, which is an intermediate product in its preparation should, they claim, have a similar structure:

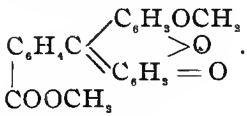


That the colorless dimethyl ether really has the structure given above cannot be doubted in view of its preparation by E. Grande[1] by a different method. He made it by the action of anisol upon phthalic anhydride in the presence of aluminum chloride, thus:



This product is identical in every respect with that obtained by Herzig and Meyer as given above.

In making the dimethyl ether of *fluoresceïn*, however, by the action of methyl iodide upon its alkaline solution, Herzig and Meyer[2] obtained a *colored* product to which the quinoid arrangement was assigned:



[1] Gazz. chim. ital., 26, 1 and 222.

[2] Loc. cit.

This would seem to favor the *quinoid* structure of the alkali salts of fluoresceïn, just as in the case of phenolphthaleïn the fact that in alkaline solution it yields with methyl iodide the *lactoid* dimethyl ether was used by the authors as an argument in favor of the lactoid structure of its alkali salts.

The same authors[1] criticize Friedländer's interpretation of the results he obtained with the oxime of phenolphthaleïn.[2] Instead of proving, as Friedländer supposed, the existence of a quinoid oxygen by forming the compound

$$\begin{array}{ll} & \diagup C_6H_4OH \\ C_6H_4C & \\ | & \diagdown C_6H_4 = NOH \\ COOH & \end{array},$$

it in reality points, they claim, to a very different conclusion. They base this criticism upon facts brought out by Friedländer, himself; *viz.*, the oxime has slight color, it forms with acetic anhydride a colorless diacetate, and dissolves in acids. Further, in acid or alkaline solutions it is reduced by zinc dust, forming a compound insoluble in acids. These facts, they say, can best be explained on the assumption that the oxime has the structure

$$\begin{array}{ll} & \diagup C_6H_4OH \\ C_6H_4\,C & \\ |\qquad\ | & \diagdown C_6H_4OH \\ CO—NOH & \end{array},$$

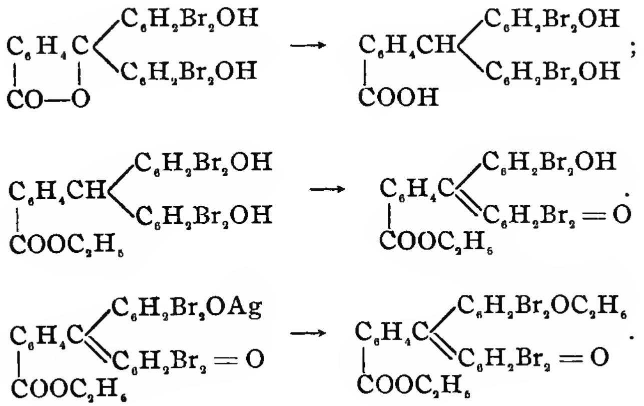
agreeing with the analogous formula first given for the anilide.[3] The product obtained by reduction and found to be insoluble in acids would be represented thus:

$$\begin{array}{ll} & \diagup C_6H_4OH \\ C_6H_4\,C & \\ |\qquad\ | & \diagdown C_6H_4OH \\ CO—NH & \end{array}.$$

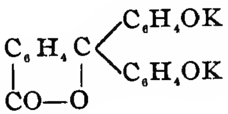
Nietzki[4] made the quinoid diethyl ether of tetrabromphenolphthaleïn by a reaction similar to that used by him in making

[1] Ber. d. chem. Ges., 28, 3258.
[2] Cf. p. 20.
[3] Cf. p. 22.
[4] Chem. Ztg., 20, 806.

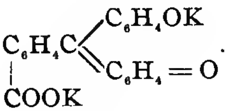
the colored diethyl ether of fluoresceïn. The phthaleïn was reduced to the corresponding phthalin, this was esterified, then oxidized to the ester of the phthaleïn, the silver salt of this with ethyl iodide yielded the colored (quinoid) diethyl ether of tetrabromphenolphthaleïn. The steps are indicated in the following formulas:



A. Bistrzycki and K. Nencki[1] have made a contribution to the question of the structure of phenolphthaleïn. They call attention to the two structures for alkali salts of phenolphthaleïn:



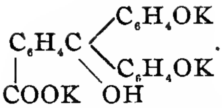
I.



II.

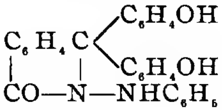
and claim that if formula I is correct, it should yield by the Baumann-Schotten reaction a *di*-benzoate insoluble in alkalies and colorless. On the other hand, if formula II be correct, then it should yield a *mono*-benzoate under the same conditions—possibly a *tri*-benzoate by the breaking up of the quinoid arrangement and becoming

[1] Ber. d. chem Ges., 29, 131.

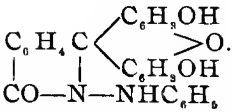


The authors found that a *di*-benzoate was formed under the conditions mentioned, colorless and insoluble in alkalies. If the compound were derived from formula II, whether it were the monobenzoate or the tribenzoate it should be soluble in alkalies. From this they advocate the lactoid structure of salts of phenolphthaleïn.

The action of phenylhydrazine upon fluoresceïn and phenolphthaleïn was investigated by Gattermann.[1] He found that when the phthaleïn was heated with phenylhydrazine, combination took place, crystals being formed that had no color and were soluble in alkalies. Not only did fluoresceïn itself react with phenylhydrazine but also fluoresceïn dichloride. He found further that the simple hydrazide of both fluoresceïn and phenolphthaleïn could be converted into dimethyl and diethyl ethers by the action of methyl iodide upon their alkaline solutions. The structure assigned by him to these hydrazides is shown in the formulas:



Phenolphthaleïn hydrazide.



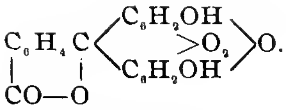
Fluoresceïn hydrazide.

It will be readily seen how in alkaline solution these compounds would yield, with methyl or ethyl iodide, diethers.

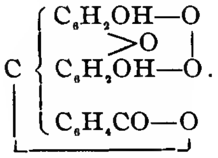
From the foregoing discussion it would seem to be clearly established that fluoresceïn and phenolphthaleïn really react as tautomeric compounds, in some cases giving lactoid derivatives, in others quinoid derivatives.

In regard to galleïn, however, it cannot be said that its structure has been determined with the same degree of certainty.. Buchka, who has done most of the woιk on galleïn, gave it the formula:

[1] Ber d. chem. Ges., 32, 1132.

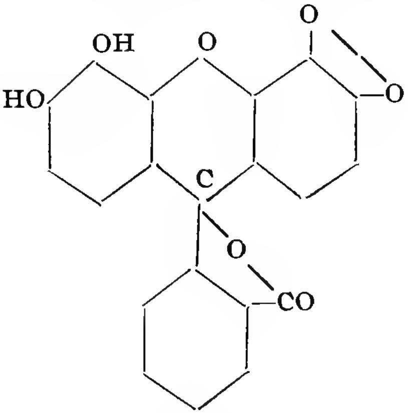


This he did by reason of his study of hydrogalleïn, a compound which Herzig, who repeated a part of Buchka's work, did not succeed in making. Schultz and Julius in their "Tabellarische Uebersicht der künstlichen organischen Farbstoffe," edition of 1891, page 98, give it the formula:



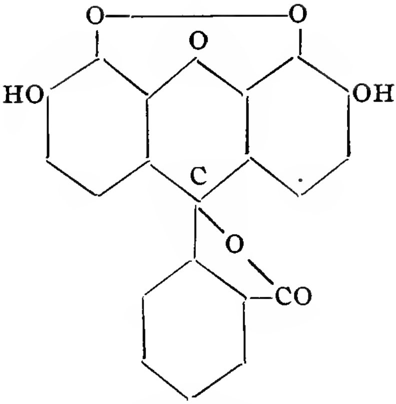
The same structure is given it in Léon Lefèvres "Matieres Colorantes Artificielle", 1896, page 1190.

Schultz and Julius, in the 1897 edition of their work, page 142, give its structure more in detail as follows:



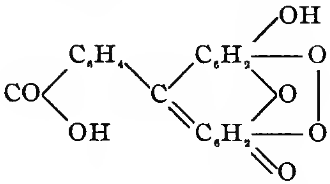
representing it, however, as orthoquinone.

Nietzki, in his "Chemie der organischen Farbstoffe" (1897), gives it the structure:



He adds, however, "Wahrscheinlich ist es fast, dass diese beiden Sauerstoffatome in einem Kern eine Orthochinongruppe bilden, auch dürfte das Galleïn zu den Chinoïden Carboxylderivaten gehören."

This idea of Nietzki's regarding the quinoid condition is contained in the structure suggested in Krafft's *Organische Chemie*, 1897, page 595, as follows:



According to this galleïn contained a quinoid, carboxyl, and quinone group.

With this diversity of opinion, it would seem important to have additional experimental evidence as to the correct formula for galleïn. This is presented in the following pages.

II. Coeruleïn.

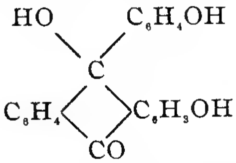
This compound also was discovered by Baeyer in 1871,[1] and was the first of the class of phthalideïns—compounds derived from phthaleïns by loss of water. He made it by the action

[1] Ber. d. chem. Ges., 4, 457.

of concentrated sulphuric acid upon galleïn at 200°C., the color of the solution changing from reddish brown to greenish brown. Coeruleïn was precipitated by pouring into water. When washed carefully and dried, it appeared as a blue-black mass.

It chars when heated giving at the same time a colorless sublimate. It is soluble in concentrated sulphuric acid with olive-brown color, from which it may be crystallized. Slightly soluble in alcohol, water, or ether, easily in glacial acetic acid with dirty green color. In hot aniline it is easily soluble with deep blue color from which it may be precipitated in blue flakes by addition of alcohol or acetic ether. Alkalies dissolve coeruleïn with green color. By reduction it yields coerulin.

Though the first phthalideïn discovered, its structure was not investigated until after that of phenolphthalideïn had been determined. Baeyer,[1] in making his investigation of phenolphthalideïn found that when heated with zinc dust, there distilled a product which proved to be phenylanthracene. He had two points to guide him in assigning to it a formula: It was derived from phenolphthaleïn by loss of water, and it gave an anthracene derivative on reduction. In view of these facts he gave it the formula:



Though containing three hydroxyl groups, he found that it gave a *di*-acetyl derivative. He explained this by saying that the anthranol hydroxyl is peculiar in being very difficult to acetylize, in this case not reacting at all.

In 1881 Buchka[2] took up the study of coeruleïn in connection with his work on galleïn. He found that it could be made not only from galleïn and sulphuric acid but also from gallin, converting it first into coerulin by sulphuric acid and oxidizing this to coeruleïn. Its properties were found to be those already assigned to it.

[1] Ann. Chem. (Liebig), 202, 90.

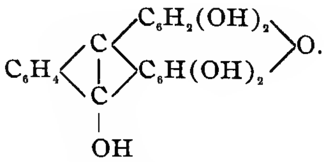
[2] *Ibid.*, 209, 258.

He prepared coeruleïn triacetate by action of acetic anhydride upon it, also by gentle oxidation of coerulin tetracetate. In this latter reaction he suggests that coeruleïn tetracetate is first formed which immediately loses one of the acetyl groups. He found that the acetate could be easily saponified by alkalies and by concentrated sulphuric acid. Its solution in acetic acid is decolorized by zinc dust, assuming, at the same time, a greenish yellow fluorescence. When diluted, yellow flakes separate which are so unstable as to make analysis impossible.

Reduction of coeruleïn in solution in ammonium hydroxide by zinc dust gives coerulin, which is easily oxidized again, even by the air, to coeruleïn. He prepared coerulin acetate by using coeruleïn and acetic anhydride with a little zinc dust. His analyses led him to pronounce the product a *tetr*acetate. He found its melting-point to be 256°. When gently oxidized it yields coeruleïn triacetate.

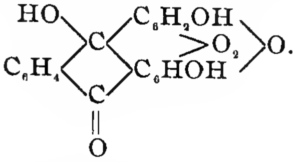
He showed the connection between coeruleïn and phenylanthracene by mixing with zinc dust and distilling in an atmosphere of hydrogen. A yellow product was obtained which crystallized from alcohol in yellow plates and when dissolved in glacial acetic acid, some potassium dichromate added and boiled, gave a product which he identified as phenyloxanthranol.

Buchka accepted the conclusion of Baeyer as to the structure of phenolphthalideïn and phenolphthalidin and assigned corresponding formulas to coeruleïn and coerulin, with some modification as to coeruleïn. Thus for coerulin he adopted the formula:

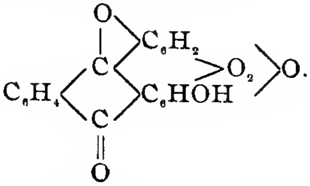


Though this formula contains five hydroxyl groups, he found that it formed a *tetr*acetate. He agreed with Baeyer in saying that the anthranol hydroxyl group was unaffected by acetic anhydride.

The formula for coeruleïn, if it be analogous to phenolphthaleïn, should be, he concludes,



But it forms an anhydride, as does rosolic acid, forming a compound to which he gives the structure:

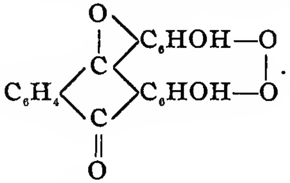


Though containing only one hydroxyl group, he found that it gave a triacetyl derivative. He assumes in this case, as in the case of galleïn, that the bond between the two quinone groups is broken. The formation of coeruleïn triacetate from coerulin tetracetate, he says, supports the formula given above for coeruleïn.

Prud'homme,[1] in his study of the reaction between coeruleïn and aniline hydrochloride, came to a different conclusion as to the number of hydroxyl groups in coeruleïn. When these two substances were heated together, condensation took place giving a derivative of coeruleïn containing *two* aniline residues. This product was found to have basic properties, and its acetate, with proper mordants, could de used as a dye, although an unsatisfactory one, since it changes color in the light. The fact that the *free base* is not fixed at all by mordants of iron, chromium, or aluminum, is used by the author to prove that it contains no hydroxyl groups. Coeruleïn, however, must contain at least *two* such groups in order to harmonize with the law of Liebermann and Kostanecki as to the coloring qualities of oxyketone dyes, that they must contain two hydroxyl groups in the *ortho* or the *para* relation to each other. If, then, the coeruleïn-aniline condensation product has *no* hy-

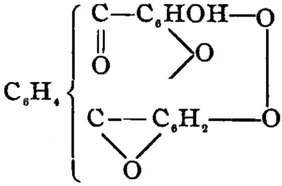
[1] Bull. Soc. chimique (Paris) (3) 11, 1136.

droxyl group, and coeruleïn has *at least two*, it follows that the aniline residue is connected with the coeruleïn molecule through its hydroxyl groups. And if the aniline residues are introduced through the hydroxyl groups and *only two residues are so introduced*, it follows that coeruleïn contains two and only two hydroxyl groups. In view of this fact, as well as its connection with galleïn, he gives coeruleïn the formula :

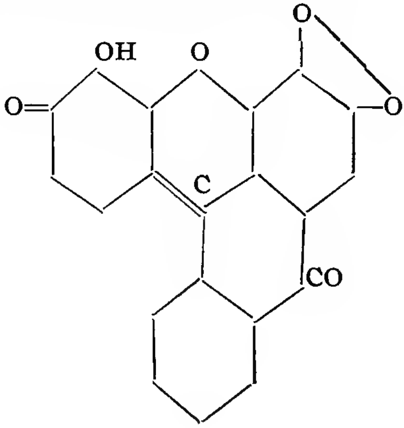


This formula also represents coeruleïn as a derivative of phenyloxanthranol.

In Schultz and Julius' "Tabellarische Uebersicht der künstlichen organischen Farbstoffe," edition of 1891, page 98, the formula for coeruleïn is given thus :



In the 1897 edition of the same work, page 142, its structure is given more in detail, as follows :



Nietzki in his "Chemie der organischen Farbstoffe," 1897, page 175, gives coeruleïn the same structure as that assigned to it by Schultz and Julius in the 1891 edition of their work quoted above. He adds, however, in a foot-note the following remark: "Eine Controlle dieser Formel wäre wohl zeitgemäss. Die vielen Sauerstoffbindungen lassen sich kaum mit den heutigen Anschauungen über derartige ringförmig constituirte Moleküle vereinigen. Auch sind die beizenfärbenden Eigenschaften bei Vorhandensein nur einer Hydroxylgruppe kaum zu erklären."

From the foregoing historical review may be gathered the development of ideas in regard to the structure of the phthaleïns and phthalideïns down to the present time. In the following pages is given an account of an investigation undertaken with a view to throwing additional light upon the subject so far as two of these are concerned—galleïn and coeruleïn.

EXPERIMENTAL.

I. GALLEÏN.

The galleïn used in this investigation was supplied by the Badische Anilin und Soda Fabrik, Ludwigshafen am Rhein, to whom grateful thanks are herewith tendered for the generous interest they have manifested in the work. It was an unusually pure product and beautifully crystallized. By transmitted light it was red, by reflected light green, with a bronzy luster. When acetylized it left no residue other than galleïn acetate.

Galleïn dissolves in an aqueous solution of pyrogallol, more easily in boiling solution, from which, after several hours, it crystallizes out. That galleïn, in addition to its marked acid properties, has slight basic properties is shown by the fact that its solubility in water or alcohol is considerably increased by the presence of an acid. This same conduct on the part of fluoresceïn was noted by Baeyer[1] and by Waddell.[2] In the case of aurin, which resembles galleïn to a marked degree,

[1] Ann. Chem. (Liebig), 183, 6.
[2] J. Phys. Chem., 2, 173.

Dale and Schorlemmer[1] have isolated a hydrochloric acid salt.[2]

When galleïn is dissolved in alcohol and an alcoholic solution of potassium hydroxide added, the potassium salt of galleïn is precipitated. It has a blue color.

Attempts were made to reduce galleïn by means of hydrogen sulphide. Solutions in ammonium hydroxide, in potassium hydroxide, sodium carbonate, and in alcohol remained unchanged after passing the gas through them for some time. Sulphur dioxide was also tried as a reducing agent, but with negative results. An alcoholic solution of galleïn remains unchanged when treated with sulphur dioxide. Galleïn in dilute caustic potash solution, when treated with sulphur dioxide, is thrown down as a dark-red precipitate, due to the neutralization of the potassium hydroxide.

An aqueous solution of galleïn, made by boiling galleïn with water and filtering the solution, treated with a solution of lead acetate or lead nitrate in water, gives first a deep-blue solution from which, finally, all the galleïn is precipitated as the basic lead salt, with indigo-blue color. This reaction is quite delicate and might be used as a test for either galleïn or lead. Galleïn does not melt or undergo any change when heated to 300° C.

Air passed through a solution of galleïn in caustic potash causes the color to change from deep-blue to brown. Hydrochloric acid added to this brown solution produces vigorous effervescence but no precipitate. It is probable that oxidation takes place here as with pyrogallol itself. This tendency of galleïn to oxidize is seen further in its action on silver nitrate, which it reduces to metallic silver.

Galleïn Tetracetate.

Galleïn tetracetate was made according to Buchka's directions—by boiling galleïn and an equal weight of sodium acetate in four times the weight of acetic anhydride for four hours. After a number of trials it was found that the acetyli-

[1] Ann. Chem. (Liebig) 196, 88.

[2] Cf. Collie and Tickle on "Salts of Dimethylpyrone and the Quadrivalence of Oxygen." J. Chem. Soc., 75 and 76, 710.

zation was complete in one hour. The excess of acetic anhydride was distilled off and the residue poured into a large amount of water. The acetate appeared on the bottom of the vessel, part as crystalline particles, part as an oil that soon solidified. The product thus obtained was filtered and when dry had a gray color; yield almost quantitative. Crystallized from benzene, it was obtained in colorless needles. Recrystallized from benzene, acetone, alcohol, and acetic acid in succession till no further change in its melting-point could be observed, it was found to melt at 241° C.[1] The melting-point as given by Buchka is 247°–248°, by Herzig[2] 236°–237°.

Galleïn acetate in a cold 5 per cent solution of sodium carbonate is insoluble; the solution remains perfectly colorless, though allowed to stand two or three days. When boiled for some time there is partial saponification, as seen by the slight purple tinge of the carbonate solution.

When treated with a few drops of concentrated sulphuric acid in the cold, galleïn acetate dissolves, giving the acid solution a deep-red color. When diluted with water the solution retains its red color, and after standing some time deposits red crystals. These crystals, when filtered out and washed with a little water, dissolve in ammonium hydroxide with the purple color and in caustic potash solution with the deep blue color so characteristic of galleïn, and give also the unmistakable test for galleïn with lead acetate. There can be no doubt that sulphuric acid saponifies the acetate and the crystals that separate are those of galleïn.

The determination of the exact constitution of galleïn acetate was an urgent matter. The difficulty of deciding it by a combustion analysis will be seen at once by a comparison of the percentages of carbon and hydrogen in galleïn acetate of different content of acetyl groups.

No. of CH_3CO groups.	C. Per cent.	H. Per cent.	Acetyl groups. Per cent.
4	63.16	3.78	32.34
5	62.72	3.84	37.48
6	62.34	3.92	41.89

[1] All melting-points were determined by means of a thermometer compared with one standardized by the Physikalisch-Technische Reichsanstalt, Charlottenburg, Germany.

[2] Monatsh. Chem., 13, 426.

From the above it will be seen that the percentage of carbon differs by about 0.4 per cent, hydrogen by about 0.07 per cent in the several cases. Buchka found C = 63.52 and 62.72, H = 4.44 and 3.82, results that agree as well with the assumption that this is a *pent*acetate as that it is a *tetr*acetate.

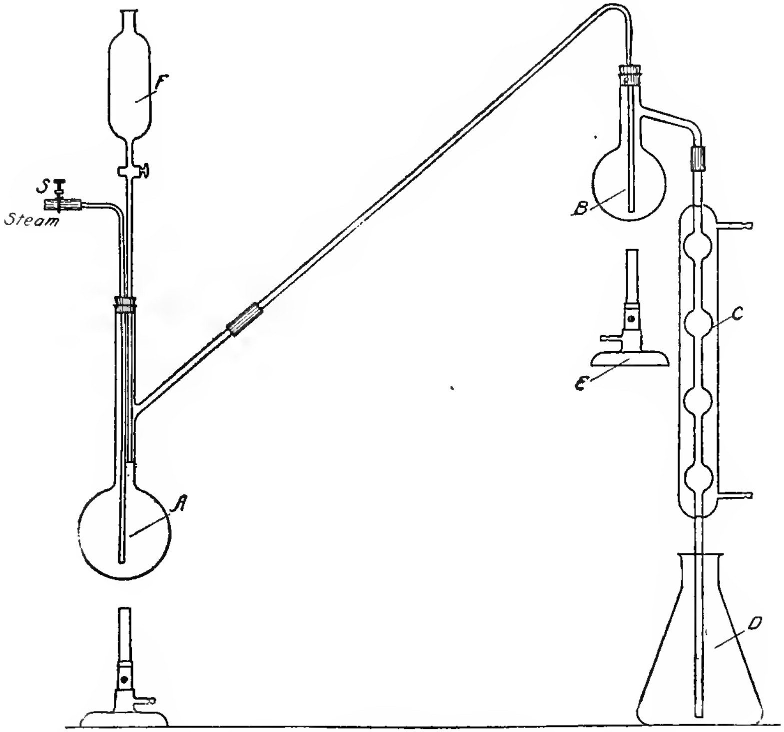
There is a much wider margin in the percentages of acetyl residues in the three supposed possible formulas, as shown in the last column in the above table. Four C_2H_3O groups would equal 32.34 per cent; five would equal 37.48 per cent, a difference of 5.14 per cent; six would equal 41.89 per cent of the whole molecule, a difference of 4.41 per cent.

Several attempts were made to determine the number of acetyl residues in the acetate by saponification by means of different alkalies, but without success, since the galleïn residue itself undergoes some decomposition when heated with alkalies giving volatile acid products that have not been further investigated. It was found, however, that a modification of Wenzel's method[1] could be used satisfactorily. The distinguishing points of this method are: First, saponification by means of strong sulphuric acid; second, removal of free sulphuric acid by means of secondary sodium phosphate; third, distillation of the liberated acetic acid *in vacuo*. The three important modifications of the Wenzel method, suggested by this work, are: First, the substitution of distillation in steam for distillation *in vacuo*; second, the abandonment of one of the condensers; third, the use of dimethylamidoazobenzene to detect and determine mineral acid in the distillate. The arrangement of the apparatus may be understood from the accompanying sketch: *A* is a 300 cc. distilling flask with delivery tube inclined upwards; *B* is a 100 cc. distilling flask with delivery tube inclined down so as to connect easily with *C*, an Allihn condenser. *D* is a 750 cc. Erlenmeyer flask, *F* a small separatory funnel, *S* a screw clamp.

A weighed amount of material is placed in *A* and 3 or 4 cc. of sulphuric acid diluted with water, two of acid to one of water by volume, run in through the funnel *F*, screw clamp *S* being closed. An excess of tenth-normal sodium hydroxide is

[1] Monatsh. Chem., 18, 659.

measured into flask *D*, the whole apparatus properly connected, and water started through the condenser. The flask *A* is then heated for one hour to the temperature of a boiling water-bath, when 3 cc. of distilled water are added and the heat continued for half an hour longer. There are now introduced 20 cc. of a solution made by dissolving 45 grams of secondary sodium



phosphate, and 10 grams of glacial phosphoric acid in 100 cc. of water. Finally, add 50 cc. of boiled distilled water, heat with a burner, and pass in steam. Liquid will soon begin to collect in flask *B*, which serves as a trap to prevent acid from being carried over mechanically. When flask *B* is one-fourth full of liquid, heat it with a burner, the heat being so regulated as to keep the liquid at a constant level. When the distillate has collected in the receiver to the amount of 600 cc.,

stop the heat and transfer the distillate to a liter measuring flask. Dilute to the mark and mix thoroughly. Measure out 500 cc. of the solution and titrate with tenth-normal HCl, using phenolphthaleïn as indicator. In order to tell whether any mineral acid (H_2SO_3, etc.) has been carried over, the remaining portion is titrated with tenth-normal HCl, using dimethylamidoazobenzene as indicator. This is sensitive to free mineral acids but not to dilute organic acids. Of course the amount of the difference between the two titrations, *i. e.* the amount of mineral acid, is to be deducted from the total amount of acid found.

The process of distillation is not yet complete. One or two cc. of tenth-normal NaOH are again measured into flask *D*, and the heating continued till 300 cc. are collected. This is titrated directly with tenth-normal HCl, using phenolphthaleïn as indicator. The total amount of acid in this distillate is so small as to make the detection of mineral acid impossible—none was discovered in it in any determination made. To make sure that all volatile acid has been driven from flask *A*, a third distillate is collected which rarely showed more than 0.2 cc. tenth-normal NaOH neutralized. The net amount of tenth-normal NaOH neutralized multiplied by 0.0043 gives the weight of acetyl groups present. This method was used in all the acetyl determinations reported in this paper.

In order to test the apparatus and chemicals, preliminary determinations were made using a compound of known composition—acetanilide. Two analyses of acetanilide were made by the method given above with the following results:

Weight of substance. Gram.	N/10 NaOH. cc.	Mineral acid.	Net N/10 NaOH.	C_2H_3O. Per cent.
0.5472	40.25	0.0	40.25	31.63
0.2260	16.85	0.0	16.85	32.05

Calculated percentage of C_2H_3O in acetanilide = 31.85.

Galleïn acetate analyzed according to this method gave the following results:

Weight of substance. Gram.	N/10 NaOH. cc.	Mineral acid.	Net N/10 NaOH. cc.	C_2H_3O. Per cent.
0.1946	15.1	0.3	14.8	32.70
0.2584	19.7	0.0	19.7	32.74

Calculated[1] for $C_{20}H_7O_7(C_2H_3O)_5$, 37.48 per cent C_2H_3O.
Calculated for $C_{20}H_8O_7(C_2H_3O)_4$, 32.34 per cent C_2H_3O.
Calculated for $C_{20}H_9O_7(C_2H_3O)_3$, 26.32 per cent C_2H_3O.

There can be no doubt from these results that this is a tetracetate of galleïn.

GALLEÏN TETRABENZOATE.

Buchka made this compound by use of benzoyl chloride. It was deemed advisable to try making it from benzoic anhydride. Galleïn (10 grams) and benzoic anhydride (50 grams) were heated to 190° C. on a metal-bath for seven hours. The melt was then transferred to a 2-liter round-bottomed flask and the excess of benzoic anhydride removed with steam. The black residue was filtered out and, after draining thoroughly, dissolved in acetone and boiled with boneblack. The acetone solution was concentrated and a little water added. In a short time yellow crystals appeared which, by repeated crystallization from acetone, alcohol, and acetic acid, became white and melted at 226°. Melting-point given by Buchka is 231°.

Efforts were made to determine the number of benzoyl residues in this compound by the method used in analyzing the acetate, but failed on account of the difficulty of completely saponifying the benzoate by sulphuric acid. But that it contains four benzoyl groups can scarcely be doubted from its analogy to the tetracetate.

HYDROGALLEÏN TETRACETATE.

The preparation of this compound from the so-called hydrogalleïn, and its identity with galleïn tetracetate, constitute the basis for Buchka's formula for galleïn. It will be remembered,

[1] In all calculations in this paper the following atomic weights have been used: O = 16, H = 1.008, C = 12.01, N = 14.04, Ag = 107.92, I = 126.85.

however, that Herzig tried to make it from Buchka's hydrogalleïn, but did not succeed.

Galleïn was dissolved in slight excess of potassium hydroxide solution, zinc dust added cautiously, and the temperature of the contents of the flask prevented from rising by a stream of cold water around the flask. When the blue color of the alkaline solution disappeared, becoming more or less brown, dilute sulphuric acid was added slowly and in such a way as to prevent an appreciable rise in temperature. The acid liquid was extracted with ether, the ether solution rapidly filtered to remove suspended particles, and dried over calcium chloride in an atmosphere of carbon dioxide. The ether solution was then distilled in a stream of carbon dioxide. An oil with a slight red color remained and on standing solidified. Acetic anhydride in excess was added and the liquid boiled, on a metal-bath, for four hours, in a flask connected with a reflux condenser. A portion of the excess of acetic anhydride was distilled off and the residue poured into water. The acetate collected on the bottom of the vessel as an oil, which afterwards solidified. The yellow product was crystallized from benzene and gave a product melting at 213°–214°. It was recrystallized from alcohol and acetic acid in succession till the melting-point was constant. The final product was colorless and melted at 216°.

The difference between this compound and galleïn acetate is seen in its conduct with sodium carbonate and concentrated sulphuric acid. This compound, when treated with a 5 per cent solution of sodium carbonate in the cold, dissolves, at once imparting to the solution at first a greenish-yellow fluorescence; the color rapidly deepens, becoming later a decided purple. The acetate, when treated with a few drops of cold concentrated sulphuric acid, dissolves with red color. When this is diluted with water it forms a *green* solution which, after standing, deposits a green precipitate. This, filtered off and washed with little water, dissolves in ammonium hydroxide with green color and in aniline with blue color, both characteristic of coeruleïn. Sulphuric acid saponifies the so-called hydrogalleïn acetate and condenses one of the products (gallin) even in the

cold, to coerulin, which is easily oxidized in alkaline solution to coeruleïn, forming a green solution with ammonium hydroxide.

Determination of the acetyl groups in this compound gave the following results :

Weight of substance. Gram.	N/10 NaOH. cc.	Mineral acid.	Net N/10 NaOH. cc.	C_2H_3O. Per cent.
0.2328	21.5	4.0	17.5	32.32
0.1690	15.7	2.75	12.95	32.95

Calculated for $C_{20}H_{11}O_7(C_2H_3O)_3$, 26.14 per cent C_2H_3O.
Calculated for $C_{20}H_{10}O_7(C_2H_3O)_4$, 32.21 per cent C_2H_3O.
Calculated for $C_{20}H_8O_7(C_2H_3O)_6$, 37.32 per cent C_2H_3O.

Clearly the compound is a tetracetate, but it has none of the characteristics of galleïn tetracetate but has all the properties of gallin tetracetate described below.

GALLIN TETRACETATE.

This compound was made by the method given by Buchka. Galleïn dissolved in ammonium hydroxide was reduced to gallin by means of zinc dust, the solution being kept at the boiling-point. After boiling thus for two hours, the purple color having disappeared, dilute sulphuric acid was added little by little through the condenser-tube till in slight excess. The acid solution was filtered while hot and cooled in an atmosphere of carbon dioxide. It was then shaken with ether to dissolve the gallin, the ether solution separated and filtered, dried over calcium chloride in an atmosphere of carbon dioxide, and finally the ether distilled off in a current of carbon dioxide. The residue, gallin, appeared as a red oil which solidified on standing. This was converted into the acetate according to details given under hydrogalleïn acetate. The crude material was recrystallized from alcohol and acetic acid and gave a colorless product melting at 216° C. Its conduct with a 5 per cent solution of sodium carbonate and with concentrated sulphuric acid was identical with that of the so-called hydrogalleïn acetate detailed above.

The difficulty of deciding the composition of hydrogalleïn (gallin) acetate by combustion analysis will appear from the

following table, which gives the percentages of carbon and hydrogen according to the different formulas :

No. of C_2H_3O groups.	C. Per cent.	H. Per cent.
3	63.41	4.06
4	62.92	4.12
5	62.50	4.15

Buchka found C = 62.72 per cent ; H = 4.37 per cent.

Determinations of the number of acetyl groups in gallin acetate resulted as follows :

Weight of substance. Gram.	N/10 NaOH. cc.	Mineral acid. cc.	Net N/10 NaGH. cc.	C_2H_3O. Per cent.
0.2490	20.3	1.5	18.8	32.46
0.1728	14.4	1.2	13.2	32.84

Calculated for $C_{20}H_{11}O_7(C_2H_3O)_3$, 26.14 per cent C_2H_3O.
Calculated for $C_{20}H_{10}O_7(C_2H_3O)_4$, 32.21 per cent C_2H_3O.
Calculated for $C_{20}H_9O_7(C_2H_3O)_5$, 37.32 per cent C_2H_3O.

In view of these results this compound is correctly called gallin tetracetate.

The residue in flask *A* (see sketch), when treated with an excess of caustic potash gives a blue color, as would be expected of gallin in presence of air.

GALLOL ACETATE.

Buchka claims to have obtained a lower reduction-product of galleïn by the use of zinc dust and acid solution. Having the formula as given by him,

$$\begin{array}{l} C_9H_4CH\left\langle \begin{array}{l} C_6H_2(OH)_2 \\ C_6H_2(OH)_2 \end{array} \right\rangle O, \\ \mid \\ CH_2OH \end{array}$$

gallol would be expected to yield a *pent*acetate. According to Buchka's method for making this substance, galleïn (5 grams) was placed in a liter flask with 700 cc. of water, a little dilute sulphuric acid added, and some zinc dust. The solution was kept boiling for ten hours, adding from time to time small

amounts of dilute acid and zinc dust. The solution lost its deep red color and became straw-yellow. It was then filtered and allowed to cool. A small deposit of crystals appeared after awhile on the bottom of the vessel. The solution was shaken with ether and the ether dried and distilled off with the same precautions as noted under hydrogalleïn acetate. A residue was left as a red oil, to which were added the crystals which had separated and the whole acetylized. The acetate was re-crystallized from alcohol, yielding colorless crystals melting sharply at 216°. Buchka's gallol pentacetate melted at 230°.

The product made as above described reacted with 5 per cent solution of sodium carbonate and with concentrated sulphuric acid in every respect as the acetates of hydrogalleïn aud gallin and could not be distinguished from them in any way. A determination of the number of acetyl groups resulted thus :

Weight of substance. Gram.	N/10 NaOH. cc.	Mineral acid. cc.	Net N/10 NaOH. cc.	C_2H_3O. Per cent.
0.2237	20.5	3.46	17.04	32.75

Calculated for $C_{20}H_{10}O_7(C_2H_3O)_4$, 32.21 per cent C_2H_3O.

A *pent*acetate, according to Buchka's formula, would have 38.25 per cent C_2H_3O. This compound not only shows all the characteristics of gallin acetate but the results obtained on analysis prove the two compounds to be identical.

An attempt was made to reduce galleïn in acetic acid solution to gallol by action of sodium amalgam, with negative results.

An effort was made to prepare gallol acetate directly from galleïn acetate. Galleïn (5 grams) is mixed with an equal weight of sodium acetate and 25 grams of acetic anhydride and boiled with a return-condenser for one hour. Zinc dust in small amounts is added from time to time, while the boiling is continued for three hours. A small quantity of the material is taken out, the acetate formed is crystallized once from alcohol and found to melt at 215°, and to dissolve in dilute ammonia with purple color. The remainder of the mixture is boiled seven hours longer, zinc dust in small quantities being added from time to time. The product crystallized once from alco-

hol melts at 214.5° and dissolves in dilute ammonia with purple color. Thus it would appear to be impossible to obtain gallol by reduction of galleïn or its acetate by zinc dust in acid solution, even with prolonged heating.

As a result of this work, however, a method for the preparation of gallin acetate was found which is very much shorter and simpler than that described by Buchka, and gives a yield almost as great as that required by theory. To 5 grams of galleïn add 5 grams of fused sodium acetate and 20 cc. of acetic anhydride. Boil with return-condenser for fifteen minutes, add 2 grams zinc dust and boil fifteen minutes longer. Allow the excess of zinc dust to settle to the bottom of the flask and pour off the solution carefully into a half liter of water. A small portion of the precipitate is granular; the bulk of it is an oil which soon solidifies, especially when agitated. Recrystallize from acetic acid, using boneblack to decolorize, afterwards from alcohol slightly diluted with water.

SILVER SALT OF GALLIN TETRACETATE.

That gallin tetracetate is an acid was shown not only by its action with dilute sodium carbonate solution but also by making its silver salt. Gallin acetate was dissolved in 95 per cent alcohol and an alcoholic solution of silver nitrate added in excess. The mixture was heated to boiling, filtered, and left in the dark for several hours. There separated a white precipitate resembling in appearance silver chloride. It was practically insoluble in alcohol when once precipitated, did not melt sharply, but decomposed when heated, and turned dark when exposed to sunlight.

The so-called gallol acetate gave rise to the same compound under the same conditions—another proof of the identity of gallin and gallol acetates.

On analysis the compound gave the following results for silver:

	Weight of substance. Gram.	Weight of Ag. Gram.	Ag. Per cent.
I	0.1044	0.0172	16.48
II	0.1072	0.0179	16.69

Calculated for $C_{20}H_8O_7(CH_3CO)_4Ag$, 16.82 per cent. Ag.

The analysis was made by placing the well-washed and dried product in a small porcelain crucible and burning out the organic matter by careful ignition.

The first analysis above was made from a product obtained from the so-called *gallol* acetate, the second from *gallin* acetate.

GALLEÏN METHYL ESTER.

This compound was made by one of the usual methods for preparation of esters. Galleïn (5 grams), methyl alcohol (30 cc)., and concentrated sulphuric acid (10 cc.) were mixed, forming a deep red solution. This was boiled with return-condenser for one and one-quarter hours when there separated a good quantity of crystals. The mass was then poured into 500 cc. water, filtered, the residue washed and dried, at first in the air, finally in an air-bath at 70°. To free the ester from any galleïn which might have been present, the ester was dissolved in ether, in which galleïn is insoluble, the solution filtered and concentrated. The ester came down in granular masses of dark red color, with bronzy luster. It dissolves in alcohol, acetone, ether, chloroform, acetic ether, with red color, but is almost insoluble in benzene. It dissolves at once in alkalies and alkaline carbonates with the colors characteristic of free galleïn in these solvents—probably owing to saponification. It did not melt when heated to 280° C.

A determination of the methoxy group by Zeisel's method in a sample dried at 100° C. resulted as follows:

Weight of ester.	Weight of AgI.	CH_3O. Per cent.
0.1819	0.1011	7.34

Calculated for one methoxy group, 8.22 per cent.

GALLEÏN ETHYL ESTER.

Galleïn (5 grams), absolute alcohol (30 cc.), concentrated sulphuric acid (20 cc.) were heated with return-condenser for two and three-quarters hours. The galleïn was entirely in solution at the beginning of the operation and, while still heating, crystals in good quantity were deposited. The mixture was poured into 500 cc. water, filtered, and washed. The es-

ter appeared as beautiful crystals, red by transmitted light, green by reflected light. It dissolves in alcohol, acetone, ether, chloroform, and acetic ether with red color. Quite a number of efforts were made to crystallize it from different solvents, but the best method of purifying it was found to be solution in anhydrous ether, filtering to remove galleïn, and concentration of the solution almost to dryness. The ester then appeared as granular masses.

Analysis of sample dried at 100° C. to constant weight gave, by Zeisel's method, the following results:

Weight of ester. Gram.	Weight of AgI. Gram.	C_2H_5O. Per cent.
0.0811	0.0518	12.25

Calculated for one ethoxy group, 11.48 per cent.

The results obtained with the methyl and the ethyl esters of galleïn indicate very clearly that galleïn is an acid and contains one carboxyl group. It is probable that what Baeyer considered alcohol of crystallization was in reality due to the presence of this ester.

GALLEÏN PHENYLCARBAMATE.

By action of phenyl isocyanate upon galleïn, combination took place, giving rise to a new compound. Galleïn dried at 100° C., and a little more than the calculated amount of phenylisocyanate were heated quickly to the boiling-point of the mixture and kept at this temperature for ten minutes—agitating from time to time. On cooling, the residue appeared as a black tar. This was taken up in benzene, the solution filtered, boiled with boneblack, and allowed to stand. A small amount of a crystalline deposit appeared which was filtered out and found to consist largely of diphenyl urea. To the filtrate, petroleum ether was added, when there appeared a bulky yellow precipitate. This was filtered out and dissolved in little chloroform. On standing, some white crystals appeared which did not saponify with caustic potash solution, and melted at 235° C., and was probably diphenyl urea. This was removed by filtration and the galleïn phenylcarbamate precipitated from the chloroform solution by petroleum ether, filtered

out, and the process of dissolving in chloroform and precipitating with petroleum ether continued till no further signs of diphenyl urea appeared.

The galleïn carbamate thus made is a solid, with light yellow color, does not melt sharply on account of decomposition, dissolves in alcohol and acetone with green fluorescence. It is an acid, as is shown by the fact that it is soluble in cold dilute sodium carbonate solution with purple color, which is changed to red by acids. The red color of the acid solution is not changed to purple by ammonia solution as would be the case were galleïn formed here. The carbamate dissolves also in cold dilute solution of ammonia with color, green by reflected light, red by transmitted light. In caustic alkali it dissolves (apparently with saponification) giving a deep-blue solution.

The nitrogen in this compound was determined by the Kjeldahl method, using Dafert's modification. A weighed amount of carbamate was placed in a 300 cc. digesting flask, 10 cc. of alcohol added to dissolve it, 30 cc. dilute sulphuric acid (1 : 5) added, and a small amount of zinc dust. The mixture was heated with return-condenser till the color disappeared (nearly). The flask was then disconnected from the condenser, and the alcohol and water evaporated till the organic matter showed first signs of charring. The remainder of the process was that of the ordinary Kjeldahl method. The following results were obtained :

	Weight of carbamate. Gram.	N/10 NH_3. cc.	Amount of N. Gram.	N. Per cent.
1	0.4274	18.0	0.025272	5.91
2	0.2711	11.4	0.0160056	5.90
3	0.1966	7.8	0.0109512	5.57
4	0.2116	8.3	0.0116532	5.51
5	0.2204	8.7	0.0122148	5.54
6	0.2372	9.35	0.0131274	5.53

Calculated for $C_{20}H_9O_7(OCNHC_6H_6)_3$, 5.83 per cent N.

Calculated for $C_{20}H_8O_7(OCNHC_6H_5)_4$, 6.68 per cent N.

Calculated for $C_{20}H_8O_7(OCNHC_6H_6)_2$ (the formula for this compound on the basis of Buchka's formula for galleïn), 4.67 per cent N.

The analyses above recorded were made from two samples which were prepared at different times—Nos. 1 and 2 from one, Nos. 3, 4, 5, and 6 from the other. The results can lead to but one conclusion, that there are three phenyl isocyanate residues introduced and that the compound is galleïn triphenylcarbamate.

GALLEÏN BASIC LEAD SALT.

A sodium carbonate solution was boiled with an excess of galleïn till there was no further evolution of gas. This solution was then filtered from the excess of galleïn and an excess of lead acetate solution added. The precipitate was filtered out and washed till the filtrate no longer gave a test for lead, and dried at 120° C. The lead compound was a dark blue powder. On analysis for lead the following results were found:

Weight of substance. Gram.	Weight of $PbSO_4$. Gram.	Pb. Per cent.
0.9343	0.8960	65.4
0.2014	0.1880	65.0

Calculated for $C_{20}H_8O_7(PbOH)_4$, 65.92 per cent Pb.

GALLEÏN TRIMETHYL ETHER.

Five grams of galleïn were dissolved in 200 cc. of methyl alcohol, 4 grams of caustic potash in 50 cc. methyl alcohol, the two solutions united, and a portion (100 cc.) of the solvent distilled off. To the residue was added methyl iodide (15 grams), and the whole heated to boiling on a water-bath for twenty to thirty hours. At intervals of about eight hours, 1 or 2 grams of solid caustic potash were added, heated for one hour, and about 5 grams methyl iodide added. The solution, at first blue, quickly becomes red. After sufficient heating the methyl alcohol and excess of methyl iodide were distilled off on a water-bath, the residue treated with 500 cc. of a 1 per cent solution of potassium hydroxide to dissolve any partially methylated products, and filtered. The residue will be considered in connection with the tetramethyl ethers.

The alkaline filtrate was acidified with a little concentrated hydrochloric acid. A yellow precipitate was thrown down

which was filtered out and washed. The dried residue was dissolved in acetone, boiled with boneblack, concentrated, a little water added, and allowed to stand. After a few hours there was a good yield of crystals which had a golden yellow color. These were then dissolved in alcohol, boiled with boneblack, concentrated, and allowed to crystallize—*little* water being added. Additional crops of crystals were obtained by further dilution of the mother-liquors. By repetition of this treatment crystals were finally obtained which were *colorless* and melted at 229°.

A determination of methoxy groups was made by Zeisel's method. Apparatus and chemicals were first tested by making a determination of the methoxy group in anisic acid, with the following result:

Weight of anisic acid. Gram.	Weight of AgI. Gram.	CH_3O. Per cent.
0.1905	0.2910	20.18

Calculated for $C_6H_4(OCH_3)COOH$, 20.39 per cent CH_3O.

The following results were obtained with the gallein ether dried at 100° C.:

Weight of ether. Gram.	Weight of AgI. Gram.	CH_3O. Per cent.
0.1866	0.3100	21.96
0.2376	0.3966	22.06

Calculated for $C_{30}H_8O_6(OCH_3)_2$ (according to Buchka's formula),[1] 13.95 per cent CH_3O.

Calculated for $C_{30}H_9O_4(OCH_3)_3$, 22.91 per cent CH_3O.

Calculated for $C_{20}H_8O_3(OCH_3)_4$, 29.55 per cent CH_3O.

The substance is hence a trimethyl ether.

Galleïn trimethyl ether dissolves in alcohol and acetone with a delicate pink tint; in benzene its solution is colorless. It resembles phenolphthaleïn quite closely. In dilute sodium carbonate solution, in dilute ammonia, as well as in caustic alkalies, it dissolves at once, even in the cold, with deep-red color.

1 The solubility of this ether in alkaline solutions is a further argument against the correctness of Buchka's formula for galleïn.

From such solutions, by the addition of acids, it is precipitated again as the *colorless* trimethyl ether.

This galleïn trimethyl ether was also made by saponification of the colored tetramethyl ether as stated below.

TRIMETHYL GALLEÏN MONOACETATE.

Galleïn trimethyl ether was mixed with an equal weight of fused sodium acetate and five times its weight of acetic anhydride, and the mixture kept at the boiling-point for one hour. The excess of acetic anhydride was distilled off and the residue poured into a large bulk of water. The precipitate was at first oily, but soon solidified. This was filtered off, and washed. The residue thus obtained was recrystallized from alcohol. The crystals were needle-shaped and colorless, showed double refraction, and were either monoclinic or triclinic. Melting-point 197°. They dissolve in alcohol, acetone, and chloroform, are insoluble in cold aqueous caustic potash, but after prolonged boiling they dissolve, giving a red color to the solution (apparently after saponification of the acetyl group). Saponification takes place more readily in alcoholic caustic potash.

The product dried at 100° C. and analyzed for methoxy groups gave the following results :

Weight of substance. Gram.	Weight of AgI. Gram.	CH_3O. Per cent.
0.2004	0.3028	19.96
0.1690	0.2570	20.08

Calculated for $C_{20}H_8O_4(OCH_3)_3(C_2H_3O)$, 20.76 per cent CH_3O.

The results of these analyses show that this derivative of galleïn contains three methoxy groups and one acetyl group. Its properties also harmonize with this view.

GALLEÏN TETRAMETHYL ETHER—COLORED.

The residue insoluble in alkalies, obtained in making trimethyl galleïn, was dissolved in 50 per cent alcohol, boiled with little boneblack to remove gummy material, concentrated,

and allowed to crystallize. Two distinct sets of crystals were deposited. One set consisted of pyramidal crystals belonging to the monoclinic system. They were red, the larger ones exhibiting a bronzy luster. By far the larger proportion of the crystals were of this sort. The others were much lighter in color and were needle-shaped. These last will be discussed under the head of galleïn tetramethyl ether—colorless.

The dark red crystals mentioned above melt sharply at 199°, dissolve in alcohol, acetone, chloroform, ether, and acetic ether, with red color. The ether is insoluble in cold alkalies, in hot alkalies it forms a red solution—after partial saponification. To an alcoholic solution of the ether a solution of sodium carbonate is added, the solution evaporated to dryness on a steam-bath, the residue dissolved in water and filtered, the filtrate acidified, there appears a precipitate with a yellow color. This is filtered out, recrystallized from alcohol, and found to be colorless and to melt at 229°. The product shows also all the other characteristics of galleïn trimethyl ether already described. The number of methoxy groups in the colored ether was determined with the following results :

Weight of substance. Gram.	Weight of AgI. Gram.	CH_3O. Per cent.
0.1770	0.3828	28.56
0.2140	0.4656	28.74

Calculated for $C_{20}H_8O_3(OCH_3)_4$, 29.55 per cent CH_3O.
Calculated for $C_{20}H_9O_4(OCH_3)_3$, 22.91 per cent CH_3O.

This ether is unquestionably a galleïn *tetra*methyl ether, and since one of the methyl groups may be split off by the action of sodium carbonate solution, leaving a product with three methyl groups (see galleïn trimethyl ether above), one of the methyl groups must replace a hydrogen atom of a carboxyl group in the form of an ester.

GALLEÏN TETRAMETHYL ETHER—COLORLESS.

The light-colored needle-shaped crystals referred to above were separated from the deep red ones, dissolved in acetic acid, boiled with bone-black, and filtered. The slightly red

solution was diluted with water till a precipitate appeared, then heated till all dissolved, and allowed to cool slowly. The crystals which separated still had some color. To remove this they were dissolved in alcohol, a little potassium hydroxide was added, and the solution heated to boiling. This saponified the colored ether, forming the potassium salt of the trimethyl ether which is easily soluble in water. The alcoholic solution diluted with water yields *colorless* crystals of the tetramethyl ether. These are needle-shaped, show double refraction, and are either monoclinic or triclinic.

The same compound was obtained by heating galleïn trimethyl ether with excess of methyl iodide in a sealed tube to 125° C. for five hours.

The colorless ether melts at 195°, is soluble in alcohol, acetone, and chloroform, but to a less degree than the colored ether. It is insoluble in aqueous caustic potash (laboratory reagent) even on boiling.

Analysis of a sample dried at 100° C. gave the following results:

Weight of substance. Gram.	Weight of AgI. Gram.	CH_3O. Per cent.
0.0804	0.1751	28.77

Calculated for $C_{20}H_8O_3(OCH_3)_4$, 29.55 per cent CH_3O.

GALLEÏN TETRAETHYL ETHER—COLORED.

Galleïn (5 grams) was dissolved in 200 cc. methyl alcohol,[1] caustic potash (4 grams) in 50 cc. of the same solvent and the two united. A portion (100 cc.) of the solvent was distilled off, and to the residue was added an excess of ethyl iodide. The color changes from blue to red. The mixture kept at the boiling-point for five to ten hours. The methyl alcohol and the excess of ethyl iodide were then distilled off on a water-bath. The residue was treated with 500 cc. of a 1 per cent solution of potassium hydroxide to dissolve any partially ethylated products, and filtered. The filtrate was used in the preparation of the triethyl ether as described below.

[1] Methyl alcohol was used in this case because it is a better solvent than ethyl alcohol for the potassium salt of galleïn.

The residue insoluble in alkali was deep red, at first a viscous mass, which slowly hardened. This was dissolved in methyl alcohol, boiled two or three times with boneblack to remove gummy impurities, concentrated, and allowed to stand several days. There appeared first needle-shaped crystals which were filtered out and are described below as the colorless tetraethyl ether. After these, in greater amount, came tabular, monoclinic crystals of a deep red color, very much like those of the colored tetramethyl ether, and melted at 155°. This ether dissolves in methyl alcohol, ethyl alcohol, acetone, chloroform, acetic ether, and acetic acid. In cold alkalies it is insoluble. If some of the ether be dissolved in alcohol, a little sodium carbonate or potassium hydroxide be added, and the mixture heated to dryness on a water-bath, it undergoes partial saponification. This was shown by dissolving the residue in water, filtering, acidifying the filtrate, when a yellow precipitate was thrown down. This product, on recrystallization, proved to be colorless, and showed the characteristics of the triether described below.

The following is the result of a determination of ethoxy groups:

Weight of substance. Gram.	Weight of AgI. Gram.	C_2H_5O. Per cent.
0.2015	0.3788	36.11
0.1199	0.2356	37.70

Calculated for $C_{20}H_8O_3(OC_2H_5)_4$, 37.82 per cent C_2H_5O.
Calculated for $C_{20}H_9O_4(OC_2H_5)_3$, 30.59 per cent C_2H_5O.

From the above analyses, as well as from the method of its preparation and its properties and reactions, this ether is the analogue of the colored galleïn tetramethyl ether.

GALLEÏN TETRAETHYL ETHER—COLORLESS.

The needle-shaped crystals referred to in connection with the colored tetraethyl ether after recrystallization from alcohol, using boneblack to decolorize, were obtained almost colorless, and found to melt at 144°. They dissolve in alcohol, acetone, acetic acid, and chloroform, but less easily than the colored variety. This ether is insoluble in aqueous alkalies, even on boiling. Analysis gave the following result for ethoxy groups:

Weight of ether. Gram.	Weight of AgI. Gram.	C_2H_5O. Per cent.
0.0682	0.1301	36.61

Calculated for $C_{20}H_8O_3(OC_2H_6)_4$, 37.82 per cent C_2H_6O.

GALLEÏN TRIETHYL ETHER.

The alkaline filtrate obtained in the preparation of galleïn tetraethyl ether was acidified with concentrated hydrochloric acid. A heavy yellow precipitate was thrown down. This was filtered out, washed well, and recrystallized from alcohol, using boneblack to decolorize. Colorless crystals were obtained which, on analysis, gave the following result:

Weight of substance. Gram.	Weight of AgI. Gram.	C_2H_5O. Per cent.
0.1057	0.1765	32.04

Calculated for $C_{20}H_9O_4(OC_2H_6)_2$, 30.59 per cent C_2H_6O.
Calculated for $C_{20}H_8O_3(OC_2H_6)_4$, 37.82 per cent C_2H_6O.

Galleïn triethyl ether dissolves easily in most of the organic solvents. In cold dilute sodium carbonate solution, in dilute ammonia, as well as in the caustic alkalies it dissolves at once with deep red color, just as phenolphthaleïn does. On acidifying these solutions the *colorless* triethyl ether is reprecipitated.

GALLIN PENTAMETHYL ETHER.

Galleïn was reduced by zinc dust in alkaline solution, and the resulting gallin extracted with ether in the usual way. After complete removal of the ether by distillation in carbon dioxide, the flask containing the residue was connected with a return condenser and also a hydrogen generator. After removing as completely as possible all air from the apparatus by means of hydrogen, a slight excess of potassium hydroxide dissolved in 95 per cent alcohol was added through the condenser tube. The solution turned light blue—due to slight oxidation. After heating five minutes an excess of methyl iodide was added and the mixture heated to boiling on a water-bath for ten hours. The alcohol and excess of methyl iodide were distilled to dryness and the residue treated with

500 cc. of a 1 per cent solution of caustic potash. The residue was filtered out, washed, and recrystallized from alcohol, using boneblack to decolorize. The crystals at first were more or less yellow, recrystallizing from alcohol and acetic acid in succession they became almost white and melted at 127°.

Analyses gave the following results :

Weight of substance. Gram.	Weight of AgI. Gram.	CH_3O. Per cent.
0.1596	0.4167	34.49
0.1877	0.4887	34.39

Calculated for $C_{20}H_9O_2(OCH_3)_6$, 35.50 per cent CH_3O.

Calculated for $C_{20}H_{10}O_3(OCH_3)_4$, 29.38 per cent CH_3O.

The compound is therefore the *penta*methyl ether of gallin.

The ether dissolves readily in alcohol, acetone, and acetic acid. It is insoluble in cold alkalies, but may be saponified by the method already outlined in connection with the galleïn colored tetra ethers, giving a product that is colorless and dissolves in alkalies without color.

II. COERULEÏN.

The coeruleïn used for the following investigation was also furnished by the Badische Anilin und Soda Fabrik, and was of exceptional purity.

It was found that if coeruleïn be pulverized and suspended in water, it could be dissolved by saturating the water with sulphur dioxide. This solution when boiled for some time to remove the gas, was decomposed and coeruleïn precipitated. When filtered out and dried, it had a beautiful bronzy lustre and seemed to be crystallized.

One marked difference between galleïn and coeruleïn is that while the former dissolves easily in solution of sodium carbonate, the latter is practically insoluble in such a solution, imparting to it only a faint yellow color even after boiling for some time.

In aniline, pyridine, and quinoline, coeruleïn dissolves, more readily if heated. In aniline it forms a deep blue solution, the color remaining unchanged in excess of acetic acid. The solution in pyridine is colored greenish blue, which turns purple

in excess of acetic acid. On boiling with quinoline the color is purple, which becomes greenish blue on cooling, and green when diluted with more quinoline.

COERULEÏN TRIACETATE.

Coeruleïn acetate was made according to the method given by Buchka—by boiling coeruleïn with sodium acetate and excess of acetic anhydride. After completion of the reäction a part of the acetic anhydride was distilled off and the residue poured into water. The red precipitate was filtered out and washed. Unsuccessful attempts were made to crystallize the acetate from glacial acetic acid, alcohol, acetone, chloroform, benzene, and acetic ether, in each of which it dissolves with red color. It was finally purified by dissolving it in acetone, filtering, evaporating to small bulk and precipitating the acetate by adding to the acetone solution a saturated solution of sodium chloride. After washing till the filtrate gave no reaction for chlorides and drying coeruleïn acetate appeared as a reddish brown powder.

That it is coeruleïn *tri*acetate cannot be doubted from the following determinations of the number of acetyl groups present :

Weight of acetate. Gram.	N/10 NaOH. cc.	Mineral acid. cc.	Net N/10 NaOH. cc.	Per cent C_2H_3O.
0.2153	16.79	2.55	14.24	28.43
0.1753	13.50	2.05	11.45	28.08

Calculated for $C_{20}H_7O_6(C_2H_3O)_3$, 27.33 per cent C_2H_3O.
Calculated for $C_{20}H_6O_6(C_2H_3O)_4$, 33.47 per cent C_2H_3O.

The difficulty of deciding by combustion analysis how many acetyl groups this compound contains, will be seen from the following table :

No. of acetyl groups.	Per cent C.	Per cent H.
3	66.10	3.39
4	65.37	3.50

Buchka found C = 65.7 and 66.71, and H = 3.75, but nevertheless calls the compound the triacetate.

COERULIN PENTACETATE.

Buchka's directions were followed in the preparation of this

compound, using 5 grams of coeruleïn, 25 grams of acetic anhydride, and a little zinc dust. After heating for twenty minutes the mass began to solidify and had a dark green color. The contents of the flask were transferred to a porcelain evaporator and heated on the water-bath till nearly all the acetic anhydride disappeared. The residue was then put into 1200 cc. water to remove all zinc salts, etc., filtered and washed. The mass was dark green. Recrystallized from glacial acetic acid, the acetate appears in greenish yellow needles which show parallel extinction and form a felted mass. Solutions of coerulin acetate in acetic acid, alcohol, acetone, and chloroform have a greenish yellow fluorescence. Buchka gives the melting-point of this compound as 256° C. This could not be verified—the compound decomposed when heated and did not melt at all.

Determinations of the number of acetyl groups in this compound resulted as follows:

Weight of acetate. Gram.	N/10 NaOH. cc.	Mineral acid. cc.	Net N/10 NaOH. cc.	Per cent C_2H_3O.
0.1837	19.9	3.05	16.85	39.44
0.1991	20.55	2.25	18.3	39.52

Calculated for $C_{20}H_8O_6(C_2H_3O)_4$, 33.34 per cent C_2H_3O.
Calculated for $C_{20}H_7O_6(C_2H_3O)_5$, 38.54 per cent C_2H_3O.

The product is therefore a *pent*acetate.

Calculated percentages of carbon and hydrogen are as follows:

No. of C_2H_3O groups.	Per cent C.	Per cent H.
4	65.11	3.87
5	64.51	3.94

Buchka found C = 65.31 and 64.64, H = 4.60 per cent, and on the bases of these analyses pronounced the compound a *tetr*acetate. In the determination of the number of acetyl groups, however, there is a much greater difference in the percentages for four and for five groups, and according to results given above for these, it cannot be doubted that the compound is in reality coerulin *pent*acetate.

COERULEÏN MONOMETHYL ETHERS.

Coeruleïn (7 grams) and potassium hydroxide (3.5 grams)

were dissolved in 150 cc. methyl alcohol and digested for one hour at the boiling-point of the mixture. There was then added an excess of methyl iodide and the whole boiled on a water-bath for twenty hours, adding at intervals of eight hours 2 grams of potassium hydroxide and boiling to make sure of solution, then slight excess of methyl iodide. The excess of methyl iodide and the methyl alcohol were then removed by distillation on water-bath, the residue treated with 500 cc. of a 1 per cent solution of potassium hydroxide, and filtered. The insoluble residue will be described below.

The alkaline filtrate was acidified and a heavy dark precipitate was thrown down and filtered out. The precipitate was dissolved in boiling alcohol, filtered, and on standing there were deposited crystals of a dark color, with bronzy luster. The compound decomposes when heated and does not melt. It dissolves in alcohol, acetone, pyridine, aniline, and potassium hydroxide solution, imparting an olive-brown color to the solution in each case.

A determination of methoxy groups gave the following result:

Weight of ether. Gram.	Weight of AgI. Gram.	CH_3O. Per cent.
0.2365	0.1703	9.51

Calculated for $C_{20}H_9O_6(OCH_3)$, 8.61 per cent CH_3O.
Calculated for $C_{20}H_8O_4(OCH_3)_2$, 16.57 per cent CH_3O.

The compound is therefore coeruleïn monomethyl ether.

The mother-liquor from which this ether was obtained was allowed to evaporate spontaneously, when another crop of crystals appeared. This compound, when dried and analyzed for methoxy groups, gave the following result:

Weight of substance. Gram.	Weight of AgI. Gram.	CH_3O. Per cent.
0.1216	0.0755	8.20

Calculated for $C_{20}H_9O_6(OCH_3)$, 8.61 per cent CH_3O.

It is clearly a coeruleïn monomethyl ether but has different properties from those of the coeruleïn ether described above. It dissolves in acetone and pyridine with a purple color, in

alcohol and aniline with a greenish-blue color, in potassiun hydroxide solution with a light-green color. It is uniforml more soluble than the isomeric compound already described.

COERULEÏN METHYL ETHER—ALKALI INSOLUBLE.

The residue insoluble in alkali (see above under coeruleï monomethyl ether) was dissolved in alcohol, the solution fil tered, and concentrated. After standing, a tarry substanc was deposited. This was filtered out and the filtrate, whicl now had a beautiful green fluorescence, allowed to stand fo some days. There appeared needle-shaped crystals which wer red by transmitted light, green by reflected light. These dis solve with some difficulty in alcohol, giving it a light purpl color, easily in concentrated sulphuric acid with red color, bu are insoluble in alkalies even on boiling. The quantity o crystals was so small as to make an analysis of the compounc impossible, but it is in all probability coeruleïn trimethyl ether

COERULEÏN MONOETHYL ETHER.

This compound was made in the same way as the mono methyl ether, using ethyl iodide and boiling only nine hours It was likewise crystallized from alcohol and had all the char acteristics of the corresponding methyl derivative. It wa dried at 100° C. and the ethoxy group determined which re sulted as follows :

Weight of ether. Gram.	Weight of AgI. Gram.	C_2H_5O. Per cent.
0.1313	0.0808	11.82

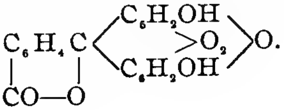
Calculated for $C_{20}H_9O_5(OC_2H_5)$, 12.04 per cent C_2H_5O.

Hence the compound is coeruleïn monoethyl ether.

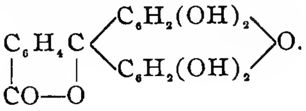
THEORETICAL.

I. GALLEÏN.

The formula for galleïn, as given by Buchka, is



It is necessary to assume with this formula that oxidation takes place in the process of making, giving rise to a quinone group. This idea was first suggested to him by the supposed discovery of the so-called hydrogalleïn, which has been regarded as a reduction-product intermediate between galleïn and gallin. Hydrogalleïn, according to Buchka, differs essentially from both galleïn and gallin, but gives the same product when acetylized as that obtained from galleïn by acetylization. In order to account for this, he gave galleïn the above formula and to hydrogalleïn the following formula :



The necessity for providing a formula for hydrogalleïn was the single consideration that led him to assign to galleïn the above formula.

Several attempts were made during the progress of this work to prepare hydrogalleïn and its acetate. The result was always the same—the hydrogalleïn acetate invariably proved to be identical in every respect with *gallin* acetate. Attempts were made also to make gallol acetate by Buchka's method—reduction of galleïn in acid solution by zinc dust, and acetylization of the product thus obtained. Here again the so-called gallol acetate was identical with *gallin* acetate. The identity of these three acetates is clearly shown not only by analysis but also by identity of melting-point and conduct with sodium carbonate solution and concentrated sulphuric acid. So that no matter whether galleïn be reduced by zinc dust in acid or alkaline solutions, hot or cold, the product is in all cases gallin, which, with acetic anhydride, yields gallin acetate. The existence of hydrogalleïn is, therefore, extremely improbable, and it is doubtful if gallol or its acetate has been isolated. The conclusions here stated with reference to hydrogalleïn is in entire accord with Herzig's work, to which reference has already been made.

That galleïn contains a carboxyl group is proved by the fact

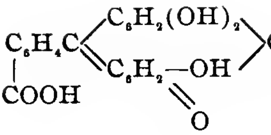
that it forms esters in the ordinary way. Methyl and ethyl esters have both been prepared. Further, galleïn forms a stable ammonium salt,[1] which suffers no loss of ammonia after prolonged heating, in this respect showing a marked difference from phenolphthaleïn. Galleïn also decomposes sodium, barium, and calcium carbonates, driving out carbon dioxide and forming soluble compounds with the metals. The presence of the carboxyl group may explain, also, why galleïn is converted more easily than other phthaleïns into its corresponding phthalideïn, since there is no necessity here for breaking the lactone ring. This will be referred to again in the theoretical discussion of coeruleïn.

The formation of the *colored* tetramethyl and tetraethyl ethers easily saponified to the *colorless* triethers with alkalies also proves the presence of a carboxyl group in galleïn. The existence of the blue basic lead salt and of the *colored* galleïn triphenyl carbamate, which has acid properties, indicates the same thing.

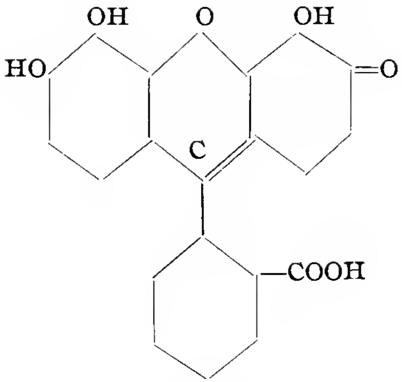
That galleïn contains only three phenol hydroxyl groups is shown by the introduction into its molecule of three phenyl isocyanate groups. It has been established, notably by Goldschmidt,[2] that phenyl isocyanate does not react with quinone oxygen, but easily with hydroxyl hydrogen, except such as are present in carboxyl groups. The galleïn triphenyl carbamate has a color and dissolves in cold solution of sodium carbonate *with color*. Hence it must contain a carboxyl group, but cannot be a derivative of gallin (formed by reduction). Since therefore Galleïn, in free condition, contains one carboxyl and three phenol hydroxyl groups, its structure must be :

1 Buchka : Ann. Chem. (Liebig), 209, 263.

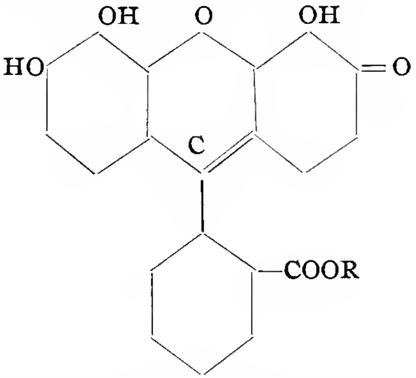
2 Ber. d. chem. Ges., 22, 3105.



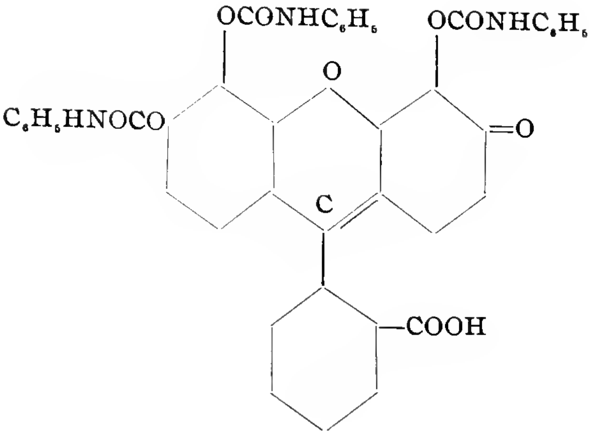
or



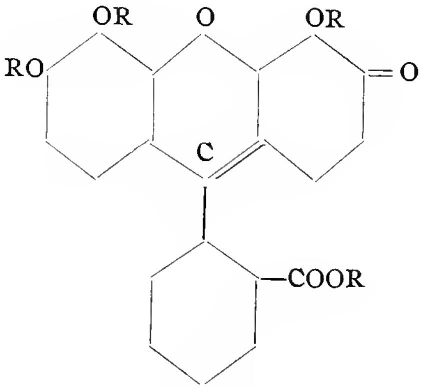
The quinoid structure would explain the deep red color of galleïn and its solutions. According to this formula, the structure of a highly colored methyl or ethyl ester would be:



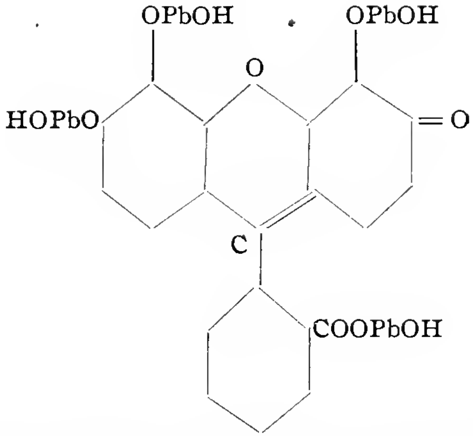
And for the colored triphenyl carbamate having acid properties:



This formula for galleïn explains also the formation and properties of its colored tetramethyl and tetraethyl ethers. These would be represented thus :

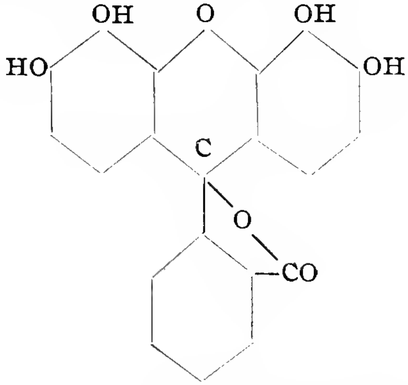


A compound with such a structure one would expect to be colored and to lose one alkyl group by saponification. As a matter of fact these ethers *are* colored (deep red), and with sodium carbonate or hydroxide saponify, leaving a trialkyl ether. The deep blue basic lead salt probably has the following formula :



and the blue potassium salt, which is precipitated when a saturated alcoholic solution of galleïn and a saturated alcoholic solution of caustic potash are mixed, probably has a similar structure, the metal potassium replacing the PbOH group.

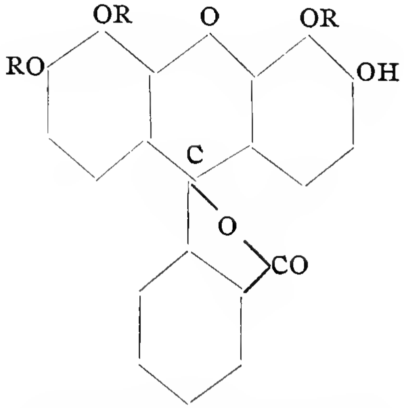
There are compounds, however, which seem to be derived from a tautomeric form of galleïn. This would have the lactoid structure and be represented thus ;



To this class belong the trimethyl and triethyl ethers which when uncombined, are colorless, but dissolve in sodium carbonate with red color. The relation between the free ethers and their alkali salts appears to be the same as that between

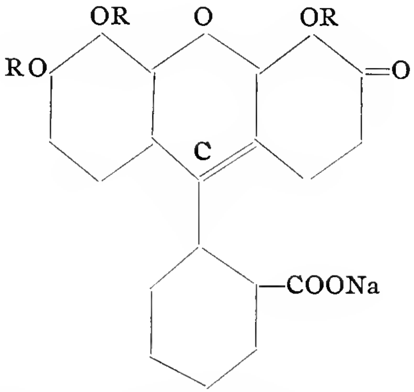
phenolphthaleïn and its salts. This relation is shown in the following formulas:

I.



Galleïn trialkyl ether. (Colorless.)

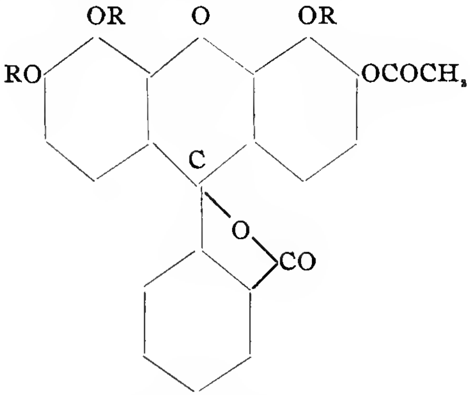
II.



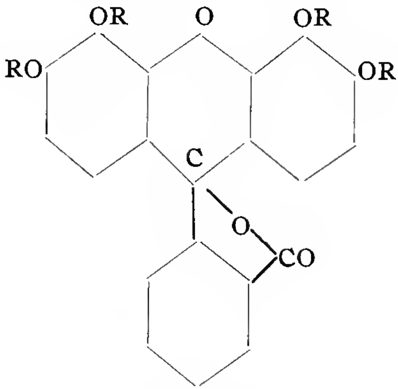
Sodium salt of galleïn tri-alkyl ether. (Red.)

That Formula I above correctly represents the structure of galleïn trialkyl ethers is indicated further by the fact that it can be readily acetylized as well as transformed into the *colorless* tetralkyl ether. The products thus obtained are also colorless. Since the labile hydrogen by this process is replaced,

the trialkyl galleïn acetate is insoluble in alkalies except on prolonged boiling, which results in saponification of the acetyl group. These characteristics accord with the following structure for the trialkyl galleïn acetate :

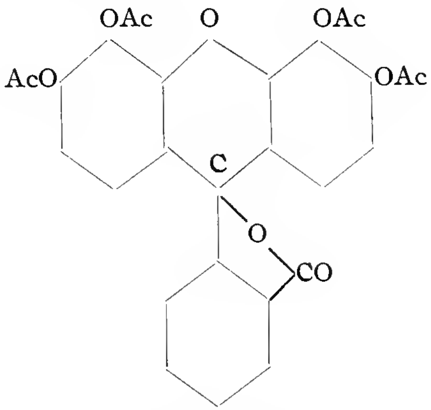


The conception of galleïn as a tautomeric substance finds support also in the existence of two classes of tetralkyl ethers—one, the quinoid (colored), already referred to ; the other, the lactoid (colorless), which would have this structure :

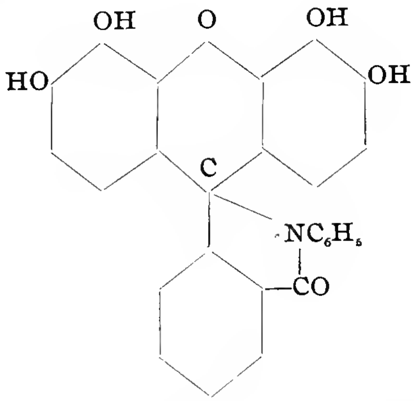


With such a structure one would expect them to be colorless and unaffected by alkalies. Both of these characteristics they were found to possess.

The acetate and the benzoate of galleïn would properly be derived from its lactoid modification, since they are colorless and (at least in the acetate) are known to contain four acid residues. Letting Ac represent the acid residue, they would have the structure :



Galleïn anilide, a colorless compound, made by Albert,[1] should be a derivative of the lactoid modification also and have the structure :



The colorless methyl ether which he made from the anilide and called a *di*methyl ether is very probably a *tetra*methyl

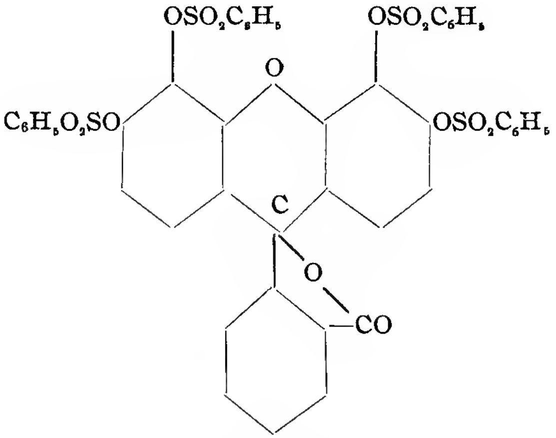
[1] Ber. d. chem. Ges., 27, 2794.

ether. By combustion analysis he found carbon = 72.72 per cent, hydrogen = 4.58 per cent.

Calculated for	Per cent C.	Per cent H.
$C_{28}H_{19}O_6N$	72.25	4.08
$C_{30}H_{25}O_5N$	72.70	5.08

From the above it is seen that this compound is more probably a *tetra*ether than a *di*ether.

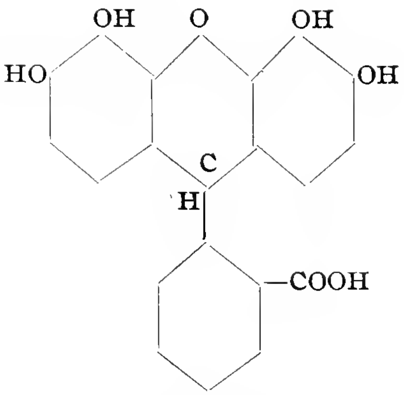
Another of the lactoid derivatives of galleïn is the tetraphenylsulphonate described by Georgescu.[1] He gives it the diketone formula which has been abandoned for all phthaleïns. It more probably has the structure:



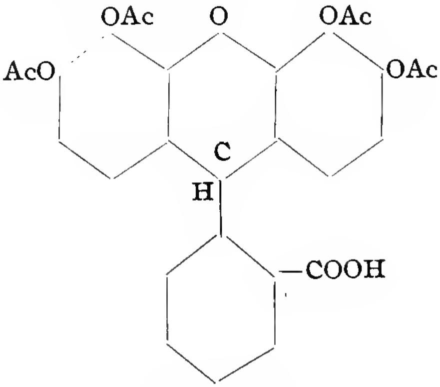
Galleïn, then, is tautomeric, yielding two classes of derivatives, those with color having the quinoid structure, and colorless derivatives with the lactoid structure. Free galleïn has the quinoid structure.

The structure of gallin is established in a measure by its relation to galleïn, from which it is derived by addition of two atoms of hydrogen. This probably breaks the quinoid arrangement with simultaneous loss of color, and the product is doubtless properly represented thus:

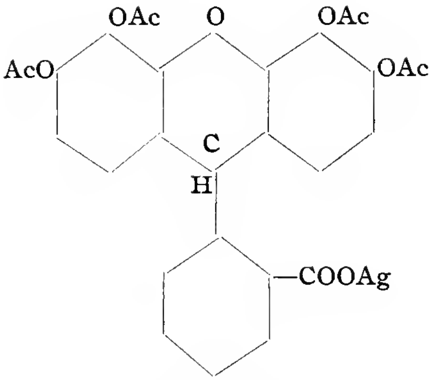
[1] Bulletinul Societătii De Sciinte, Fizice, 1, 215.



In support of this view of its structure is its easy transformation into the colorless tetracetate, a compound with acid properties. This characteristic it shows not only in dissolving readily in sodium carbonate solution, but also in forming a silver salt. The structure of gallin acetate and its silver salt is shown in the following formulas :

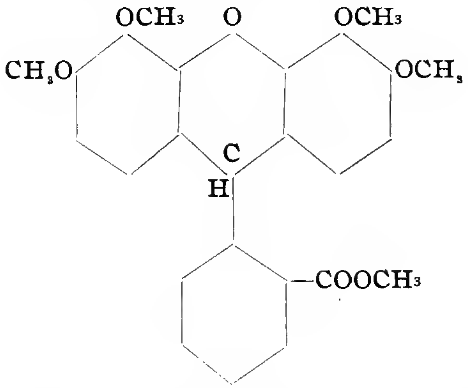


Gallin acetate.



Silver salt of gallin acetate.

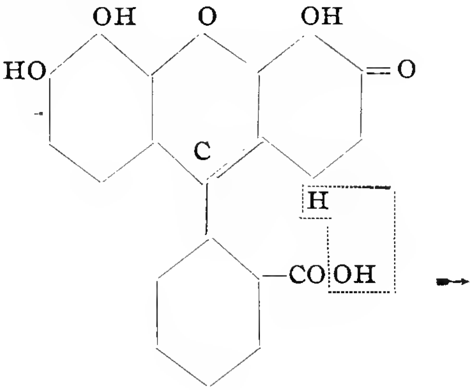
A further proof of the correctness of this view of the structure of gallin is the formation of a *penta*methyl derivative by action of methyl iodide upon an alkaline solution of gallin. It probably has the following structure :

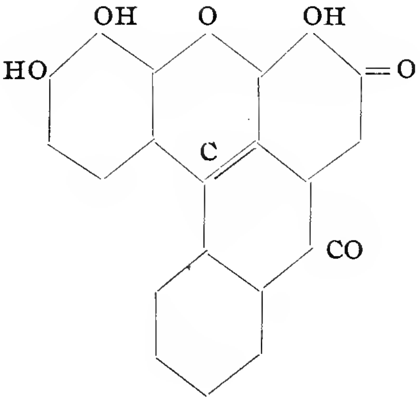


As was to be expected, this ether, though insoluble in cold alkalies, may be saponified by heating in alkali solutions, forming a product easily soluble in sodium carbonate without color.

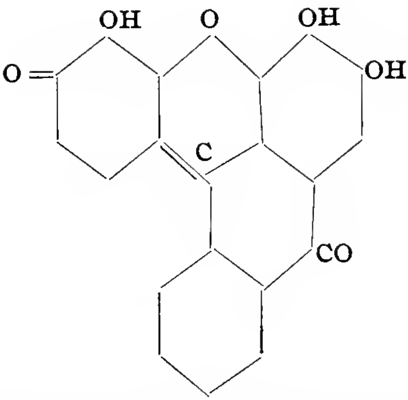
II. COERULEÏN.

Coeruleïn is the phthalideïn of galleïn and sustains to it the same relation as that between phenolphthaleïn and phenolphthalideïn. Baeyer, in his work on phenolphthalideïn, found that when it was distilled with zinc dust, it yields phenylanthracene. Buchka obtained the same product by distilling coeruleïn with zinc dust. Since coeruleïn is derived from galleïn, probably by the loss of one molecule of water, and since, according to Buchka's work, it contains the phenylanthracene group, it would seem that the hydroxyl group of the phthalic acid residue in galleïn unites with one of the hydrogen atoms of one of the pyrogallol residues to form water, the readjustment of affinities taking place as represented in the following formulas:

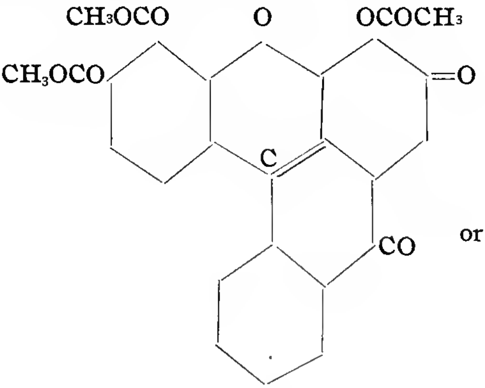




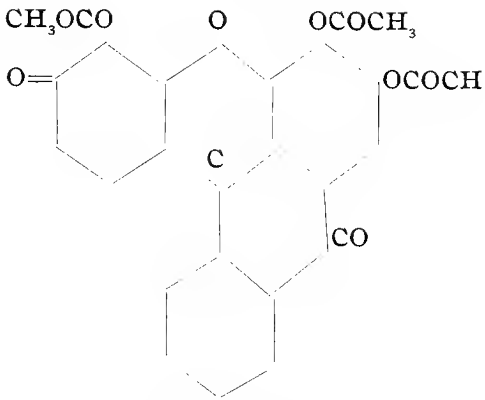
or



That the carboxyl group of galleïn takes part in the reaction is indicated by the fact that, while galleïn is easily soluble in sodium carbonate solution, coeruleïn is practically insoluble in such a solution. The presence of a carboxyl group in galleïn explains the easy formation of coeruleïn, compared with other phthalideïns. This formula is also in accord with the fact that when all the oxygen atoms are replaced in coeruleïn by hydrogen by means of zinc dust, phenylanthracene is formed. It easily explains how coeruleïn forms a triacetate easily reduced with zinc dust in acetic acid solution. Such a derivative would be represented thus:

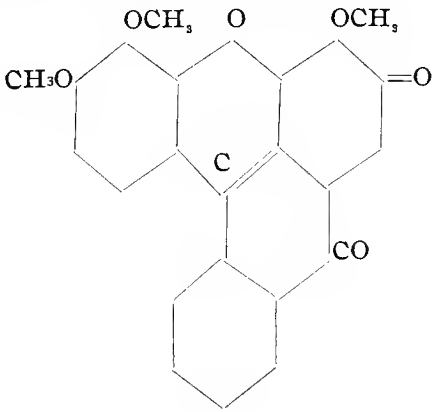


or

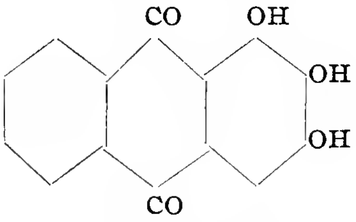


With the formula given above for coeruleïn there is a possibility of having three varieties of monoalkyl ethers. Two monomethyl ethers are described in the experimental part of this paper. It is impossible at present to determine the exact position of the methyl group in these ethers. They are readily soluble in alkalies—a characteristic they could not show if only one hydroxyl group were present in coeruleïn as represented in Buchka's formula for this compound. Again the fact that there are two monoethers requires that more than one hydroxyl group be present in the molecule.

A methyl ether was made, which was entirely insoluble in alkalies, even boiling, but in such small amounts as to make analysis impossible. This was probably coeruleïn trimethyl ether. It would have the structure:

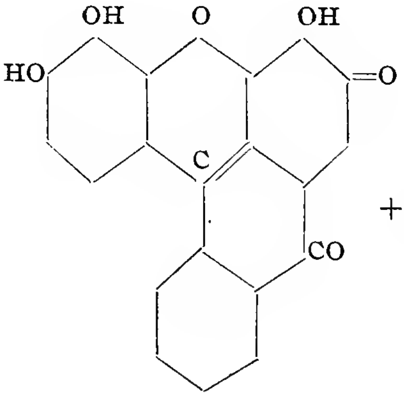


Coeruleïn thus appears as a derivative of anthragallol,

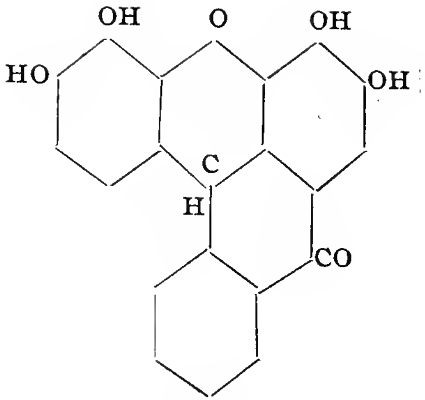


which, like coeruleïn, is soluble in alkalies with a green color. This will explain why coeruleïn resembles alizarin and anthragallol in its property of forming insoluble lakes with chromium, iron, and aluminium mordants. The name, alizarin green, by which coeruleïn is known, recalls this fact, which has long been known to the dyer. The above formula for coeruleïn also serves to recall the aurin group of dyestuffs, to which it shows certain resemblances.

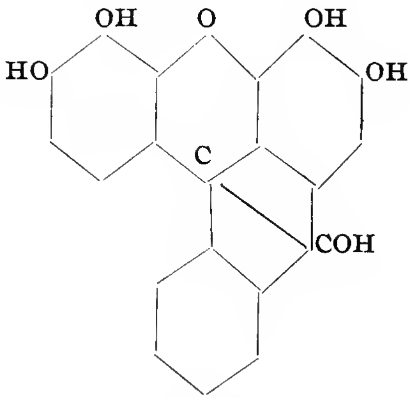
Coerulin is derived from coeruleïn by addition of two hydrogen atoms. This would probably result first in breaking the quinoid group, thus:



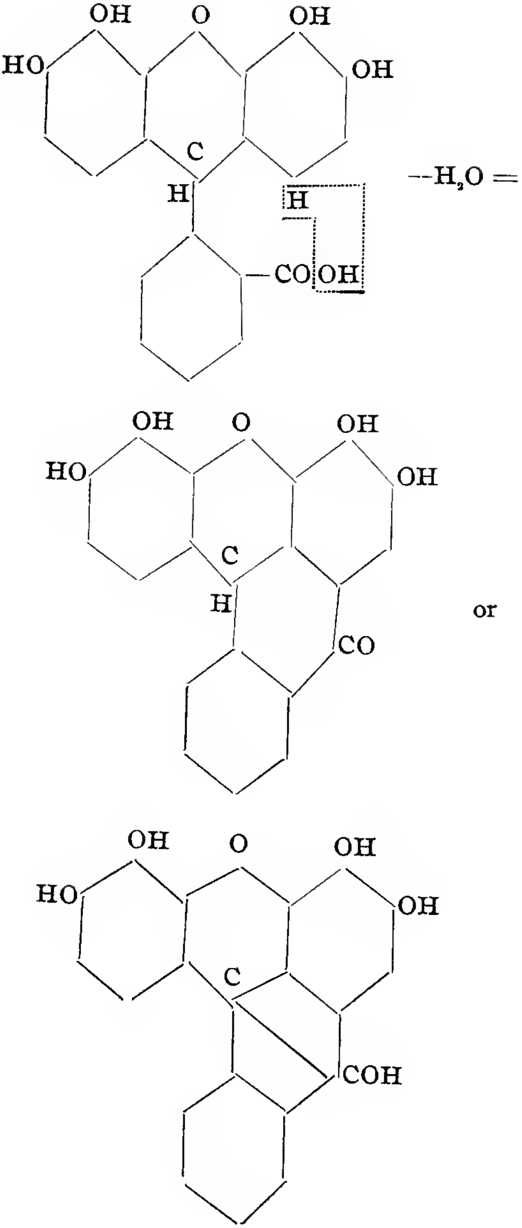
$+ 2H =$



The reduced product would be expected to go over to the more stable form and become:



Coerulin is formed also from gallin by the action of concentrated sulphuric acid in the cold. The transformation may be represented thus:


OH
O
OH
HO
OH
C
H
H
CO
OH
$-H_2O =$
OH
O
OH
HO
OH
C
H
CO
or
OH
O
OH
HO
OH
C
COH

In favor of this view of the structure of coerulin is the fact that it forms a *pent*acetate with acetic anhydride.

The more important facts brought out in this paper may be found in the following summary :

SUMMARY.

1. The only reduction product of galleïn by zinc dust, whether in acid or alkaline solution, is gallin.

2. Galleïn forms monoesters, showing that it contains one carboxyl group.

3. Three phenyl isocyanate groups may be introduced into a molecule of galleïn, proving that it contains three phenol hydroxyl groups.

4. Two classes of tetralkyl ethers, colored and colorless, are derivable from galleïn, indicating that it reacts in tautomeric modifications.

5. Colorless trialkyl derivatives of galleïn are described.

6. A colorless trimethyl galleïn acetate is described.

7. Gallin pentamethyl ether furnishes evidence as to the structure of gallin.

8. A silver salt of gallin acetate also furnishes evidence as to the structure of gallin.

9. Coeruleïn is shown to form a triacetate—by determination of its acetyl groups.

10. Coeruleïn forms two monomethyl ethers, and a methyl ether insoluble in alkalies. Likewise a monoethyl ether.

11. Coerulin forms a pentacetate, as shown by a determination of its acetyl groups.